```
=> fil reg; d ide l1
FILE 'REGISTRY' ENTERED AT 16:03:58 ON 16 JAN 2002
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STRUCTURE FILE UPDATES:   15 JAN 2002  HIGHEST RN 383362-48-9
DICTIONARY FILE UPDATES:  15 JAN 2002  HIGHEST RN 383362-48-9

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Calculated physical property data is now available.  See HELP PROPERTIES
for more information.  See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf



L1   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2002 ACS
RN   54-11-5  REGISTRY
CN   Pyridine, 3-[(2S)-1-methyl-2-pyrrolidinyl]- (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   Nicotine (8CI)
CN   Pyridine, 3-(1-methyl-2-pyrrolidinyl)-, (S)-
OTHER NAMES:
CN   (-)-.beta.-Pyridyl-.alpha.-N-methylpyrrolidine
CN   (-)-3-(1-Methyl-2-pyrrolidyl)pyridine
CN   (-)-Nicotine
CN   (S)-(-)-Nicotine
CN   (S)-3-(1-Methyl-2-pyrrolidinyl)pyridine
CN   (S)-Nicotine
CN   Flux Maag
CN   L-Nicotine
CN   l-Nicotine
CN   Nicoderm
CN   Niconil
CN   Nicorette
CN   Nicotin
CN   Nicotinell
CN   XL All Insecticide
FS   STEREOSEARCH
DR   13890-81-8, 13890-82-9, 6912-85-2, 551-13-3, 16760-37-5
MF   C10 H14 N2
CI   COM
LC   STN Files:   ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,
       BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN,
       CHEMCATS, CHEMINFORMRX, CHEMLIST, CHEMSAFE, CIN, CSCHEM, CSNB, DDFU,
       DETHERM*, DIOGENES, DRUGNL, DRUGU, DRUGUPDATES, EMBASE, GMELIN*, HODOC*,
       HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT,
       NIOSHTIC, PDLCOM*, PHAR, PHARMASEARCH, PIRA, PROMT, RTECS*, SPECINFO,
       TOXCENTER, TOXLIT, TULSA, ULIDAT, USAN, USPAT2, USPATFULL, VETU
         (*File contains numerically searchable property data)
     Other Sources:   DSL**, EINECS**, TSCA**
         (**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.  Rotation (-).
```
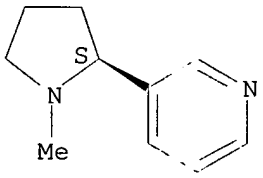



514/343

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

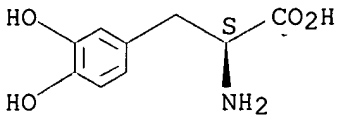
10364 REFERENCES IN FILE CA (1967 TO DATE)
212 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
10380 REFERENCES IN FILE CAPLUS (1967 TO DATE)
3 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> d ide l2; d ide l3; d ide l5

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN 59-92-7 REGISTRY
CN L-Tyrosine, 3-hydroxy- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Alanine, 3-(3,4-dihydroxyphenyl)-, L- (8CI)
OTHER NAMES:
CN (-)-3,4-Dihydroxyphenylalanine
CN (-)-Dopa
CN .beta.-(3,4-Dihydroxyphenyl)-.alpha.-L-alanine
CN .beta.-(3,4-Dihydroxyphenyl)-L-alanine
CN .beta.-(3,4-Dihydroxyphenyl)alanine
CN 3,4-Dihydroxy-L-phenylalanine
CN 3,4-Dihydroxyphenyl-L-alanine
CN 3,4-Dihydroxyphenylalanine
CN 3-(3,4-Dihydroxyphenyl)-L-alanine
CN 3-Hydroxy-L-tyrosine
CN DA
CN Dihydroxy-L-phenylalanine
CN DOPA
CN Dopaflex
CN Dopalina
CN Dopar
CN Dopaston
CN Dopaston SE
CN Eldopal
CN Helfo-dopa
CN Insulamina
CN L-(-)-Dopa
CN L-.beta.-(3,4-Dihydroxyphenyl)-.alpha.-alanine
CN L-3-(3,4-Dihydroxyphenyl)alanine
CN L-4,5-Dihydroxyphenylalanine
CN L-DOPA
CN Larodopa
CN Levodopa
CN Levopa
CN Pardopa
FS STEREOSEARCH
DR 25525-15-9, 23734-74-9, 72572-99-7, 72573-00-3, 90638-38-3, 88250-23-1, 34241-25-3
MF C9 H11 N O4
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS,

CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGU,
EMBASE, GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE,
MRCK*, NAPRALERT, NIOSHTIC, PHARMASEARCH, PROMT, RTECS*, SPECINFO,
SYNTHLINE, TOXCENTER, TOXLIT, USAN, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**, NDSL**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



514/567

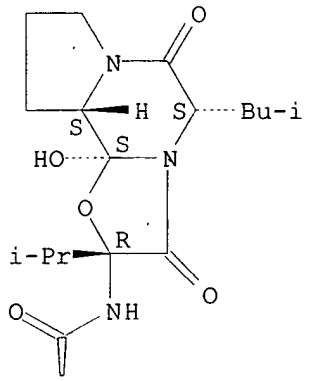
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

9364 REFERENCES IN FILE CA (1967 TO DATE)
264 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
9375 REFERENCES IN FILE CAPLUS (1967 TO DATE)
17 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L3 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN 25614-03-3 REGISTRY
CN Ergotaman-3',6',18-trione, 2-bromo-12'-hydroxy-2'-(1-methylethyl)-5'-(2-methylpropyl)-, (5'.alpha.)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 8H-Oxazolo[3,2-a]pyrrolo[2,1-c]pyrazine, ergotaman-3',6',18-trione deriv.
CN Ergocryptine, 2-bromo- (8CI)
CN Indolo[4,3-fg]quinoline, ergotaman-3',6',18-trione deriv.
OTHER NAMES:
CN .alpha.-Bromoergocryptine
CN 2-Bromo-.alpha.-ergocryptine
CN 2-Bromo-.alpha.-ergokryptine
CN 2-Bromoergocryptine
CN Bromergocryptine
CN Bromocriptin
CN Bromocriptine
CN Bromocryptine
CN Bromoergocryptine
CN SAN 15-754
CN Sandoz 15-754
FS STEREOSEARCH
DR 127931-09-3, 148043-11-2, 26409-15-4, 47830-26-2
MF C32 H40 Br N5 O5
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGPAT, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, NAPRALERT, NIOSHTIC, PHAR, PIRA, PROMT, RTECS*, SPECINFO, TOXCENTER, TOXLIT, USAN, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

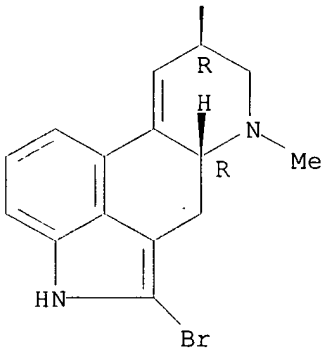
Absolute stereochemistry.

PAGE 1-A



514/250

PAGE 2-A

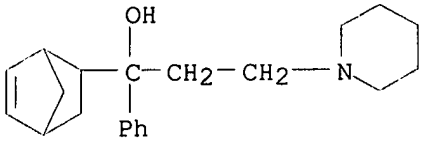


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2182 REFERENCES IN FILE CA (1967 TO DATE)
8 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2184 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L5 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN 514-65-8 REGISTRY
CN 1-Piperidinepropanol, .alpha.-bicyclo[2.2.1]hept-5-en-2-yl-.alpha.-phenyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1-Piperidinepropanol, .alpha.-5-norbornen-2-yl-.alpha.-phenyl- (6CI, 7CI, 8CI)

OTHER NAMES:
CN .alpha.-(Bicyclo[2.2.1]hept-5-en-2-yl)-.alpha.-phenyl-1-piperidinopropanol
CN .alpha.-5-Norbornen-2-yl-.alpha.-phenyl-1-piperidinepropanol
CN Akineton
CN Akinophyl
CN Piperiden
CN KL 373
FS 3D CONCORD
DR 107629-33-4
MF C21 H29 N O
CI COM
LC STN Files: ADISNEWS, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CHEMLIST, CIN, DDFU, DIOGENES, DRUGU, EMBASE, IPA, MEDLINE, MRCK*, PHARMASEARCH, PROMT, RTECS*, SPECINFO, TOXCENTER, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



514/319

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

227 REFERENCES IN FILE CA (1967 TO DATE)
6 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
227 REFERENCES IN FILE CAPLUS (1967 TO DATE)
18 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

```
=> fil medl
FILE 'MEDLINE' ENTERED AT 17:08:15 ON 17 JAN 2002

 FILE LAST UPDATED: 2 JAN 2002 (20020102/UP). FILE COVERS 1958 TO DATE.

 On April 22, 2001, MEDLINE was reloaded. See HELP RLOAD for details.

 MEDLINE now contains IN-PROCESS records. See HELP CONTENT for details.

 MEDLINE is now updated 4 times per week. A new current-awareness alert
 frequency (EVERYUPDATE) is available. See HELP UPDATE for more information.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2001 vocabulary. Enter HELP THESAURUS for details.

 The OLDMEDLINE file segment now contains data from 1958 through 1965.
 Enter HELP CONTENT for details.

 Left, right, and simultaneous left and right truncation are available in the
 Basic Index. See HELP SFIELDS for details.

 THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE
 SUBSTANCE IDENTIFICATION.

=> d que l119; d que l128; s l119 or l128; fil embase; d que l163; d que l170; s l163 or
l170; fil capl
L116(     11074)SEA FILE=MEDLINE ABB=ON  NICOTINE/CT
L117(     19873)SEA FILE=MEDLINE ABB=ON  PARKINSON DISEASE/CT
L118(      2032)SEA FILE=MEDLINE ABB=ON  TOURETTE SYNDROME/CT
L119          5 SEA FILE=MEDLINE ABB=ON  L116 AND L117 AND L118

L120(     11074)SEA FILE=MEDLINE ABB=ON  NICOTINE/CT
L121(     19873)SEA FILE=MEDLINE ABB=ON  PARKINSON DISEASE/CT
L122(      2032)SEA FILE=MEDLINE ABB=ON  TOURETTE SYNDROME/CT
L123(      2148)SEA FILE=MEDLINE ABB=ON  L120(L)(AD OR TU)/CT
L124(      9887)SEA FILE=MEDLINE ABB=ON  L121(L)TH./CT
L125(       835)SEA FILE=MEDLINE ABB=ON  L122(L)TH./CT
L126(       906)SEA FILE=MEDLINE ABB=ON  L123/MAJ
L127(      6978)SEA FILE=MEDLINE ABB=ON  L124/MAJ OR L125/MAJ
L128         16 SEA FILE=MEDLINE ABB=ON  L126 AND L127

L204         20 L119 OR L128

FILE 'EMBASE' ENTERED AT 17:08:38 ON 17 JAN 2002
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 FILE COVERS 1974 TO 10 Jan 2002 (20020110/ED)

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 substance identification.

L159(     14399)SEA FILE=EMBASE ABB=ON  NICOTINE/CT
L160(     19031)SEA FILE=EMBASE ABB=ON  PARKINSON DISEASE/CT
L161(      1965)SEA FILE=EMBASE ABB=ON  GILLES DE LA TOURETTE SYNDROME/CT
```

Subheadings
AD - administration & dosage
TU - therapeutic use
TH - therapy

Subheading DT - drug therapy

```
L162(       686)SEA FILE=EMBASE ABB=ON  L159(L)DT/CT
L163          5 SEA FILE=EMBASE ABB=ON  L162 AND L160 AND L161

L164(     14399)SEA FILE=EMBASE ABB=ON  NICOTINE/CT
L165(     19031)SEA FILE=EMBASE ABB=ON  PARKINSON DISEASE/CT
L166(      1965)SEA FILE=EMBASE ABB=ON  GILLES DE LA TOURETTE SYNDROME/CT
L167(       686)SEA FILE=EMBASE ABB=ON  L164(L)DT/CT
L168(       498)SEA FILE=EMBASE ABB=ON  L167/MAJ
L169(    358814)SEA FILE=EMBASE ABB=ON  GENERAL REVIEW/DT
L170          8 SEA FILE=EMBASE ABB=ON  L168 AND (L165 OR L166) AND L169

L205          9 L163 OR L170

FILE 'CAPLUS' ENTERED AT 17:08:39 ON 17 JAN 2002
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26, 1996), unless otherwise indicated in the original publications.

FILE COVERS 1907 - 17 Jan 2002  VOL 136 ISS 3
FILE LAST UPDATED: 16 Jan 2002  (20020116/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

  This file supports REG1stRY for direct browsing and searching of
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  more information.

CAplus now provides online access to patents and literature
covered in CA from 1907 to the present.  Bibliographic
information and abstracts were added in 2001 for over 3.8
million records from 1907-1966.

CAS roles have been modified effective December 16, 2001. Please
check your SDI profiles to see if they need to be revised. For
information on CAS roles, enter HELP ROLES at an arrow prompt or use
the CAS Roles thesaurus (/RL field) in this file.

The CA Lexicon is now available in the Controlled Term (/CT) field.
Enter HELP LEXICON for full details.

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=> d que l14; fil drugu; d que l53; d que l61; s l53 or l61; fil wpids;d que l115
L1             1 SEA FILE=REGISTRY ABB=ON  NICOTINE/CN
L4         10494 SEA FILE=CAPLUS ABB=ON  L1
L7          9453 SEA FILE=CAPLUS ABB=ON  PARKINSON?/OBI
L8          2162 SEA FILE=CAPLUS ABB=ON  ANTIPARKINSON?/OBI
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L10         344 SEA FILE=CAPLUS ABB=ON  TOURETTE?/OBI
L11         488 SEA FILE=CAPLUS ABB=ON  L4(L)THU/RL
L14          10 SEA FILE=CAPLUS ABB=ON  L11(L)(L7 OR L8 OR L10)
```

Role
THU - therapeutic use

```
FILE 'DRUGU' ENTERED AT 17:09:18 ON 17 JAN 2002
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FILE LAST UPDATED: 11 JAN 2002      <20020111/UP>
>>>  DERWENT DRUG FILE (SUBSCRIBER)  <<<

>>>  SDI'S MAY BE RUN WEEKLY OR MONTHLY AS OF JUNE 2001.  <<<
>>>  (WEEKLY IS THE DEFAULT). FOR PRICING INFORMATION     <<<
>>>  SEE HELP COST                                        <<<

>>>  FILE COVERS 1983 TO DATE  <<<
>>>  THESAURUS AVAILABLE IN /CT  <<<


L48        1186 SEA FILE=DRUGU ABB=ON  NICOTINE *PH/CT OR NICOTINE *TR/CT
L52         187 SEA FILE=DRUGU ABB=ON  GILLES-DE-LA-TOURETTE-SYNDROME/CT
L53          12 SEA FILE=DRUGU ABB=ON  L48 AND L52


L1            1 SEA FILE=REGISTRY ABB=ON  NICOTINE/CN
L48        1186 SEA FILE=DRUGU ABB=ON  NICOTINE *PH/CT OR NICOTINE *TR/CT
L49        3165 SEA FILE=DRUGU ABB=ON  PARKINSONISM/CT
L50        2799 SEA FILE=DRUGU ABB=ON  ANTIPARKINSONIAN/CT
L60         734 SEA FILE=DRUGU ABB=ON  L1
L61          11 SEA FILE=DRUGU ABB=ON  L49 AND L48 AND L50 AND L60


L206         23 L53 OR L61


FILE 'WPIDS' ENTERED AT 17:09:20 ON 17 JAN 2002
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FILE LAST UPDATED: 14 JAN 2002              <20020114/UP>
MOST RECENT DERWENT UPDATE            200203   <200203/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> SDI'S MAY BE RUN ON EVERY UPDATE OR MONTHLY AS OF JUNE 2001.
    (EVERY UPDATE IS THE DEFAULT). FOR PRICING INFORMATION
    SEE HELP COST <<<

>>> FOR UP-TO-DATE INFORMATION ABOUT THE DERWENT CHEMISTRY
    RESOURCE, PLEASE VISIT
         http://www.derwent.com/chemistryresource/index.html <<<

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES,
    SEE http://www.derwent.com/dwpi/updates/dwpicov/index.html <<<


L82        2089 SEA FILE=WPIDS ABB=ON  NICOTINE
L86        6527 SEA FILE=WPIDS ABB=ON  ?PARKINSON?
L87         608 SEA FILE=WPIDS ABB=ON  TOURETTE?
L105        297 SEA FILE=WPIDS ABB=ON  L82 (5A)(TREAT? OR THERAP?)
L108         68 SEA FILE=WPIDS ABB=ON  L105(S)ADDICT?
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L110      21549 SEA FILE=WPIDS ABB=ON  WITHDRAWAL OR ABUSE
L111         90 SEA FILE=WPIDS ABB=ON  L105(S)L110
L113        158 SEA FILE=WPIDS ABB=ON  L105 NOT (L108 OR L111)
L114         51 SEA FILE=WPIDS ABB=ON  L105(S)(L86 OR L87)
L115         11 SEA FILE=WPIDS ABB=ON  L113 AND L114


=> dup rem l204,l14,l205,l206,l115
FILE 'MEDLINE' ENTERED AT 17:09:45 ON 17 JAN 2002

FILE 'CAPLUS' ENTERED AT 17:09:45 ON 17 JAN 2002
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FILE 'WPIDS' ENTERED AT 17:09:45 ON 17 JAN 2002
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PROCESSING COMPLETED FOR L204
PROCESSING COMPLETED FOR L14
PROCESSING COMPLETED FOR L205
PROCESSING COMPLETED FOR L206
PROCESSING COMPLETED FOR L115
L207         61 DUP REM L204 L14 L205 L206 L115 (12 DUPLICATES REMOVED)
               ANSWERS '1-20' FROM FILE MEDLINE
               ANSWERS '21-28' FROM FILE CAPLUS
               ANSWERS '29-36' FROM FILE EMBASE
               ANSWERS '37-52' FROM FILE DRUGU
               ANSWERS '53-61' FROM FILE WPIDS

=> d ibib ab hitrn 1-61

L207 ANSWER 1 OF 61     MEDLINE                          DUPLICATE 2
ACCESSION NUMBER:    2001524316     MEDLINE
DOCUMENT NUMBER:     21455616   PubMed ID: 11571330
TITLE:               Transdermal nicotine in PD: a randomized, double-blind,
                     placebo-controlled study.
AUTHOR:              Vieregge A; Sieberer M; Jacobs H; Hagenah J M; Vieregge P
CORPORATE SOURCE:    Department of Neurology, University Hospital of Lubeck,
                     Germany.
SOURCE:              NEUROLOGY, (2001 Sep 25) 57 (6) 1032-5.
                     Journal code: NZ0; 0401060. ISSN: 0028-3878.
PUB. COUNTRY:        United States
                     (CLINICAL TRIAL)
                     Journal; Article; (JOURNAL ARTICLE)
                     (RANDOMIZED CONTROLLED TRIAL)
LANGUAGE:            English
FILE SEGMENT:        Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH:         200110
ENTRY DATE:          Entered STN: 20010926
                     Last Updated on STN: 20011022
                     Entered Medline: 20011018
AB   BACKGROUND: An inverse association between cigarette smoking and the risk
     of idiopathic PD has been found in many epidemiologic studies. The
     therapeutic and possible neuroprotective effects of nicotine formulations
     on parkinsonian symptoms are controversial. METHODS: In a 12-week,
     randomized, double-blind, placebo-controlled trial, the efficacy and
     tolerability of transdermal nicotine patches as an add-on treatment for
```

cardinal symptoms were evaluated in 32 nonsmoking patients with PD. After a 1-week run-in phase, patients were randomized to receive nicotine patches (containing 17.5 mg nicotine in the first and 35.0 mg nicotine in the second and third weeks) or identically appearing placebo patches. After this treatment, 3 weeks without patch application followed. The same blinded examiner assessed the patients with the Columbia University Rating Scale, the Webster scale, the Schwab-England scale, a timed walking test, with an instrumental test for fine motor skills and hand tremor, and with the Hamilton Depression Scale. RESULTS: No significant drug effects between both groups were observed in any of the scores and quantitative tests. Side effects were mild and comparable in frequency between both groups. CONCLUSIONS: With the dosage and the period of treatment chosen, transdermal nicotine patches are not effective as an add-on treatment for symptoms of PD.

L207 ANSWER 2 OF 61 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 97476729 MEDLINE
DOCUMENT NUMBER: 97476729 PubMed ID: 9336013
TITLE: Nicotine for the treatment of Tourette's syndrome.
AUTHOR: Sanberg P R; Silver A A; Shytle R D; Philipp M K; Cahill D W; Fogelson H M; McConville B J
CORPORATE SOURCE: Department of Surgery, University of South Florida College of Medicine, Tampa 33612-4799, USA.
SOURCE: PHARMACOLOGY AND THERAPEUTICS, (1997) 74 (1) 21-5. Ref: 51
Journal code: P44; 7905840. ISSN: 0163-7258.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199711
ENTRY DATE: Entered STN: 19971224
Last Updated on STN: 19971224
Entered Medline: 19971114

AB Recent evidence has demonstrated that nicotine may obtund the symptoms of Tourette's syndrome (TS). TS is a neuropsychiatric disorder characterized by motor and vocal tics, obsessions and compulsions, and frequently with impulsivity, distractibility, and visual-motor deficits. While neuroleptics, such as haloperidol, are most effective for treatment of the motor and vocal tics of TS, these medications have many side effects. In this article, we review the evidence, consistent with findings in animals, that administration of nicotine (either 2 mg nicotine gum or 7 mg transdermal nicotine patch) potentiates the therapeutic properties of neuroleptics in treating TS patients and that a single patch may be effective for a variable number of days. These findings suggest that transdermal nicotine could serve as an effective adjunct to neuroleptic therapy for TS.

L207 ANSWER 3 OF 61 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 97039779 MEDLINE
DOCUMENT NUMBER: 97039779 PubMed ID: 8991874
TITLE: [Nicotine in neuropsychiatric movement disorders].
Nikotin bei neuropsychiatrischen Bewegungsstorungen.
AUTHOR: Erdmann R
CORPORATE SOURCE: Abteilung Klinische Psychiatrie und Psychotherapie der Medizinischen Hochschule Hannover.
SOURCE: FORTSCHRITTE DER NEUROLOGIE-PSYCHIATRIE, (1996 Sep) 64 (9) 362-6. Ref: 42
Journal code: F67; 8103137. ISSN: 0720-4299.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)

(REVIEW, TUTORIAL)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199701
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19970114

AB Nicotine has various effects in the CNS, especially in dopaminergic and cholinergic systems, relevant in pathophysiology of neuropsychiatric movement disorders. Nicotine acutely reduce the symptomatology in Parkinson's disease. In neuroleptic-induced Parkinsonism (NIP) acute nicotine application induces positive changes of symptomatology. Chronic application, however, leads to a greater likelihood of NIP. The results concerning tardive dyskinesia are not consistent, but nicotine tends to exercise a positive influence on basic mechanisms. In the Gilles-de-la-Tourette syndrome nicotine reduces the severity and frequency of the tics given in combination with haloperidol.

L207 ANSWER 4 OF 61 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 95167070 MEDLINE
DOCUMENT NUMBER: 95167070 PubMed ID: 7862924
TITLE: Nicotine may relieve symptoms of Parkinson's disease.
AUTHOR: Fagerstrom K O; Pomerleau O; Giordani B; Stelson F
CORPORATE SOURCE: Pharmacia Research Laboratories, Helsingborg, Sweden.
SOURCE: PSYCHOPHARMACOLOGY, (1994 Sep) 116 (1) 117-9.
Journal code: QGI; 7608025. ISSN: 0033-3158.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
(CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199503
ENTRY DATE: Entered STN: 19950404
Last Updated on STN: 19990129
Entered Medline: 19950323

AB Two elderly patients with Parkinson's disease were treated with nicotine gum and patch. Reliable changes in symptomatology were noted, using a single-subject, placebo-control reversal design. Improvement was associated with active nicotine dosing and involved diminished tremor and disorganized thinking in one patient and diminished bradykinesia and increased energy in the other.

L207 ANSWER 5 OF 61 MEDLINE DUPLICATE 11
ACCESSION NUMBER: 89280990 MEDLINE
DOCUMENT NUMBER: 89280990 PubMed ID: 2567480
TITLE: Nicotine and cannabinoids as adjuncts to neuroleptics in the treatment of Tourette syndrome and other motor disorders.
AUTHOR: Moss D E; Manderscheid P Z; Montgomery S P; Norman A B; Sanberg P R
CORPORATE SOURCE: Laboratory of Psychobiochemistry, University of Texas El Paso 79968.
CONTRACT NUMBER: RR 08012 (NCRR)
SOURCE: LIFE SCIENCES, (1989) 44 (21) 1521-5. Ref: 18
Journal code: L62; 0375521. ISSN: 0024-3205.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198907

ENTRY DATE: Entered STN: 19900309
Last Updated on STN: 19970203
Entered Medline: 19890720

AB Animal studies suggest nicotine and cannabinoids may significantly enhance the therapeutic value of neuroleptics in motor disorders. This was recently demonstrated in humans by the finding that chewing nicotine gum produced striking relief from tics and other symptoms of Tourette syndrome not controlled by neuroleptic treatment alone. It appears that the use of nicotine or cannabinoids may greatly improve the clinical response to neuroleptics in motor disorders.

L207 ANSWER 6 OF 61 MEDLINE
ACCESSION NUMBER: 2000400739 MEDLINE
DOCUMENT NUMBER: 20313851 PubMed ID: 10857708
TITLE: The effects of nicotine on Parkinson's disease.
AUTHOR: Kelton M C; Kahn H J; Conrath C L; Newhouse P A
CORPORATE SOURCE: Department of Psychiatry, College of Medicine, University of Vermont, USA.
CONTRACT NUMBER: M01-00109
SOURCE: BRAIN AND COGNITION, (2000 Jun-Aug) 43 (1-3) 274-82.
Journal code: AM9; 8218014. ISSN: 0278-2626.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000901
Last Updated on STN: 20000901
Entered Medline: 20000823

AB Post-mortem studies have demonstrated a substantial loss of nicotinic receptors in Parkinson's disease (PD), which may be at least partially responsible for some of the cognitive, motoric, and behavioral deficits seen in this disorder. Epidemiologic studies have suggested that cigarette smoking is a strong negative risk factor for the development of PD. We have previously shown that blockade of central nicotinic receptors produces cognitive impairment in areas of new learning, short-term memory, and psychomotor slowing with increasing dose sensitivity with age and disease. Studies of acute stimulation of nicotinic receptors in Alzheimer's disease with nicotine and the novel agonist ABT-418 in our laboratory and others have shown improvements in several measures of cognitive function. Prior studies of the effects of nicotine in PD have suggested some improvements in clinical symptomatology. We have begun quantitative studies of both acute and chronic nicotine in PD to assess both cognitive and motor effects. Fifteen (15) nondemented subjects (age 66 +/- 5.3; M/F = 11/4) with early to moderate PD (mean Hoehn-Yahr stage = 1.77; MMSE = 28.6) received a dose-ranging study of intravenous nicotine up to 1.25 microg/kg/min, followed by chronic administration of nicotine by transdermal patch with doses ranging up to 14 mg per day for 2 weeks. Testing occurred both during drug administration and up to 2 months after drug cessation to look for prolonged effects. Preliminary analysis shows improvements after acute nicotine in several areas of cognitive performance, particularly measures such as reaction time, central processing speed, and decreased tracking error. Improvements in attention and semantic retrieval were not seen. After chronic nicotine, improvements were seen in several motor measures suggesting improved extrapyramidal functioning. This appeared to be sustained for up to 1 month after drug. The treatment was well tolerated. Nicotinic stimulation may have promise for improving both cognitive and motor aspects of Parkinson's disease.

L207 ANSWER 7 OF 61 MEDLINE
ACCESSION NUMBER: 2000433056 MEDLINE
DOCUMENT NUMBER: 20340862 PubMed ID: 10880717
TITLE: Nicotine, brain nicotinic receptors, and neuropsychiatric

disorders.
AUTHOR: Mihailescu S; Drucker-Colin R
CORPORATE SOURCE: Departamento de Fisiologia, Facultad de Medicina, and, Instituto de Fisiologia Celular, Universidad Nacional Autonoma de Mexico (UNAM), Mexico, D.F., Mexico.
SOURCE: ARCHIVES OF MEDICAL RESEARCH, (2000 Mar-Apr) 31 (2) 131-44.
Ref: 222
Journal code: BIC; 9312706. ISSN: 0188-4409.
PUB. COUNTRY: Mexico
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 20000928
Last Updated on STN: 20000928
Entered Medline: 20000918

AB Neuronal nicotinic acetylcholine receptors (nAChRs) represent a large family of ligand-gated cation channels with diverse structures and properties. In contrast to the muscular nAChRs, the physiological functions of neuronal nAChRs are not well defined to date. Behavioral studies indicate that brain nAChRs participate in complex functions such as attention, memory, and cognition, whereas clinical data suggest their involvement in the pathogenesis of certain neuropsychiatric disorders (Alzheimer's and Parkinson's diseases, Tourette's syndrome, schizophrenia, depression, etc.). For the majority of these disorders, the use of nAChRs' agonists may represent either a prophylactic (especially for Alzheimer's and Parkinson's diseases) or a symptomatic treatment. The possible mechanisms underlying these beneficial effects as well as the characteristics and potential therapeutic use of new, subtype-selective nAChRs agonists are presented.

L207 ANSWER 8 OF 61 MEDLINE
ACCESSION NUMBER: 1999305667 MEDLINE
DOCUMENT NUMBER: 99305667 PubMed ID: 10377904
TITLE: Can nicotine help Parkinson's?.
AUTHOR: Anonymous
SOURCE: JOHNS HOPKINS MEDICAL LETTER, HEALTH AFTER 50, (1999 Jun) 11 (4) 8.
Journal code: C24; 9802902. ISSN: 1042-1882.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: K
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 19990714
Last Updated on STN: 19990714
Entered Medline: 19990629

L207 ANSWER 9 OF 61 MEDLINE
ACCESSION NUMBER: 1999088607 MEDLINE
DOCUMENT NUMBER: 99088607 PubMed ID: 9871441
TITLE: Role of excitatory amino acids in the ventral tegmental area for central actions of non-competitive NMDA-receptor antagonists and nicotine.
AUTHOR: Svensson T H; Mathe J M; Nomikos G G; Schilstrom B
CORPORATE SOURCE: Department of Physiology and Pharmacology, Karolinska Institutet, Stockholm, Sweden.
SOURCE: AMINO ACIDS, (1998) 14 (1-3) 51-6.
Journal code: C77; 9200312. ISSN: 0939-4451.
PUB. COUNTRY: Austria
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199901
ENTRY DATE: Entered STN: 19990128
Last Updated on STN: 19990128
Entered Medline: 19990113

AB The putative role of non-NMDA excitatory amino acid (EAA) receptors in the ventral tegmental area (VTA) for the increase in dopamine (DA) release in the nucleus acumbens (NAC) and the behavioural stimulation induced by systemically administered dizocilpine (MK-801) was investigated. Microdialysis was utilized in rats with probes in the VTA and NAC. The VTA was perfused with the AMPA and kainate receptor antagonist CNQX (0.3 or 1.0 mM) or vehicle and dialysates from the NAC were analyzed with high-performance liquid chromatography for DA. Forty min after onset of CNQX or vehicle perfusion of the VTA MK-801 (0.1 mg/kg) was injected subcutaneously (s.c.). Subsequently, typical MK-801 induced behaviours were assessed. The MK-801 induced hyperlocomotion was associated with a 50% increase of DA levels in NAC dialysates. Both the MK-801 evoked hyperlocomotion and DA release in the NAC were effectively antagonized by CNQX perfusion of the VTA. However, by itself the CNQX or vehicle perfusion of the VTA did not affect DA levels in NAC or the rated behaviours. The results indicate that MK-801 induced hyperlocomotion and increased DA release in the NAC are largely elicited within the VTA via activation of non-NMDA EAA receptors, tentatively caused by locally increased EAA release. In contrast, the enhanced DA output in the NAC induced by systemic nicotine (0.5 mg/kg s.c.) was not antagonized by intra VTA infusion of CNQX (0.3 or 1.0 mM), but instead by infusion of the NMDA receptor antagonist AP-5 (0.3 or 1.0 mM) into the VTA, which by itself did not alter DA levels in the NAC. Thus, the probably indirect, EAA mediated activation of the mesolimbic DA neurons in the VTA by MK-801 and nicotine, respectively, seems to be mediated via different glutamate receptor subtypes.

L207 ANSWER 10 OF 61 MEDLINE
ACCESSION NUMBER: 97245082 MEDLINE
DOCUMENT NUMBER: 97245082 PubMed ID: 9089841
TITLE: Differential effects of transdermal nicotine on microstructured analyses of tics in Tourette's syndrome: an open study.
AUTHOR: Dursun S M; Reveley M A
CORPORATE SOURCE: Department of Psychiatry, Faculty of Medicine, University of Leicester.
SOURCE: PSYCHOLOGICAL MEDICINE, (1997 Mar) 27 (2) 483-7.
Journal code: QER; 1254142. ISSN: 0033-2917.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199706
ENTRY DATE: Entered STN: 19970716
Last Updated on STN: 19970716
Entered Medline: 19970627

AB BACKGROUND: The treatment of Tourette's syndrome (TS) is often unsatisfactory. However, there is some evidence that transdermal nicotine patch (TNP) application may improve tics of nonsmoking TS patients who are refractory to haloperidol treatment. METHODS: In this open study we applied two 10 mg TNP for 2 consecutive days to four TS patients whose symptoms were not controlled by haloperidol and to a never-medicated TS patient, all of whom are non-smokers. The Yale Global Tic Severity Scale (YGTSS) and a quantified video-taped micro-structured analysis of tics (head-shake tics, eye-blinks, vocal tics, facial grimace and other body tics) were both carried out to assess the change after the application of TNP. RESULTS: TNP application significantly reduced the YGTSS by an

average of 50%, with no reported side-effects, for up to 4 weeks but not 16 weeks, as compared with TNP-free period. Consistent with these results, the total counts of tics also showed a significant decrease for up to 4 weeks after the TNP application. CONCLUSION: TNP application differentially affected individually quantified tics, which may suggest a differential role of nicotinic receptors in the generation of different tics.

L207 ANSWER 11 OF 61 MEDLINE
ACCESSION NUMBER: 1998057792 MEDLINE
DOCUMENT NUMBER: 98057792 PubMed ID: 9396010
TITLE: Nicotinic acetylcholine receptors in health and disease.
AUTHOR: Lindstrom J
CORPORATE SOURCE: Department of Neuroscience, Medical School of the University of Pennsylvania, Philadelphia 19104-6074, USA.
CONTRACT NUMBER: NS11323 (NINDS)
SOURCE: MOLECULAR NEUROBIOLOGY, (1997 Oct) 15 (2) 193-222. Ref: 135
Journal code: AH6; 8900963. ISSN: 0893-7648.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199801
ENTRY DATE: Entered STN: 19980129
Last Updated on STN: 19980129
Entered Medline: 19980113

AB Nicotinic acetylcholine receptors (AChRs) are a family of acetylcholine-gated cation channels that form the predominant excitatory neurotransmitter receptors on muscles and nerves in the peripheral nervous system. AChRs are also expressed on neurons in lower amounts throughout the central nervous system. AChRs are even being reported on unexpected cell types such as keratinocytes. Structures of these AChRs are being determined with increasing precision, but functions of some orphan subunits are just beginning to be established. Functional roles for postsynaptic AChRs in muscle are well known, but in neurons the post-, peri-, extra-, and presynaptic roles of AChRs are just being revealed. Pathogenic roles of AChRs are being discovered in many diseases involving mechanisms ranging from mutations, to autoimmune responses, to the unknown; involving cell types ranging from muscles, to neurons, to keratinocytes; and involving signs and symptoms ranging from muscle weakness to epilepsy, to neurodegenerative disease, to psychiatric disease, to nicotine addiction. Awareness of AChR involvement in some of these diseases has provoked new interests in development of therapeutic agonists for specific AChR subtypes and the use of expressed cloned AChR subunits as possible immunotherapeutic agents. Highlights of recent developments in these areas will be briefly reviewed.

L207 ANSWER 12 OF 61 MEDLINE
ACCESSION NUMBER: 97158826 MEDLINE
DOCUMENT NUMBER: 97158826 PubMed ID: 9006184
TITLE: Does nicotine have beneficial effects in the treatment of certain diseases?.
AUTHOR: Birtwistle J; Hall K
CORPORATE SOURCE: University of Southampton, Department of Psychiatry, Royal South Hants Hospital.
SOURCE: BRITISH JOURNAL OF NURSING, (1996 Oct 24-Nov 13) 5 (19) 1195-202. Ref: 69
Journal code: BIG; 9212059. ISSN: 0966-0461.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Nursing Journals
ENTRY MONTH: 199702
ENTRY DATE: Entered STN: 19970219
Last Updated on STN: 19980206
Entered Medline: 19970206

AB Although tobacco smoking has long been associated with diseases of the lungs and cardiovascular system, numerous studies have demonstrated a negative association between tobacco smoking and ulcerative colitis, and the neurodegenerative diseases, Alzheimer's disease (AD) and Parkinson's disease (PD). The evidence suggests that nicotine--the main pharmacologically active ingredient of tobacco--appears to be responsible for this effect. Pure nicotine has no known carcinogenic properties and can be administered in numerous ways including transdermal patches and tablets. As a therapeutic agent, its association with tobacco can be likened to morphine and opium smoking. There is ample clinical evidence to suggest that nicotine could be beneficial in the treatment of some patients with diseases. Pharmacologically, nicotine acts on cholinergic (nicotinic-specific) receptors which are depleted in AD and PD. Nicotinic receptors also interact closely with several neurotransmitters including dopamine, which is implicated in both PD and Gilles de la Tourettes's syndrome. There is no doubt that tobacco smoking can be harmful and no-one should be encouraged to smoke. However, although nicotine has many harmful side-effects, it may have therapeutic value or at the very least be a useful tool for future drug development.

L207 ANSWER 13 OF 61 MEDLINE
ACCESSION NUMBER: 97003923 MEDLINE
DOCUMENT NUMBER: 97003923 PubMed ID: 8851234
TITLE: [Nicotine and Tourette's syndrome].
Nikotin und Tourette-Syndrom.
AUTHOR: Erdmann R; Schneider U
CORPORATE SOURCE: Medizinische Hochschule Hannover Abteilung Klinische Psychiatrie und Psychotherapie.
SOURCE: PSYCHIATRISCHE PRAXIS, (1996 Jan) 23 (1) 41-2.
Journal code: QCK; 0423204. ISSN: 0303-4259.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19961216

L207 ANSWER 14 OF 61 MEDLINE
ACCESSION NUMBER: 95166307 MEDLINE
DOCUMENT NUMBER: 95166307 PubMed ID: 7862206
TITLE: Nicotine as a therapeutic drug.
AUTHOR: Westman E C; Levin E D; Rose J E
CORPORATE SOURCE: Nicotine Research Laboratory, Veterans Affairs Medical Center, Durham.
SOURCE: NORTH CAROLINA MEDICAL JOURNAL, (1995 Jan) 56 (1) 48-51.
Ref: 39
Journal code: NTX; 2984805R. ISSN: 0029-2559.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW LITERATURE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 199503
ENTRY DATE: Entered STN: 19950404
Last Updated on STN: 19980206
Entered Medline: 19950322

AB Current evidence about the therapeutic potential of nicotine is strongest for ulcerative colitis. The role, if any, of nicotine therapy in Parkinson's or Alzheimer's diseases is not clear, but further research appears warranted. We need more information about the tolerability and safety of nicotine administration in such diseases. At present, any therapeutic trials of nicotine therapy should occur only as part of research protocols. Further nonjudgmental examination of the perceived effects of tobacco use may lead to other uses of nicotine. However, given the widespread morbidity and mortality directly attributable to tobacco use, no form of tobacco should be used to deliver nicotine. We encourage everyone who uses tobacco products to quit.

L207 ANSWER 15 OF 61 MEDLINE
ACCESSION NUMBER: 95075164 MEDLINE
DOCUMENT NUMBER: 95075164 PubMed ID: 7983976
TITLE: Longlasting improvement of Tourette's syndrome with transdermal nicotine.
AUTHOR: Dursun S M; Reveley M A; Bird R; Stirton F
SOURCE: LANCET, (1994 Dec 3) 344 (8936) 1577.
Journal code: L0S; 2985213R. ISSN: 0140-6736.
PUB. COUNTRY: ENGLAND: United Kingdom
Letter
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199501
ENTRY DATE: Entered STN: 19950116
Last Updated on STN: 19950116
Entered Medline: 19950103

L207 ANSWER 16 OF 61 MEDLINE
ACCESSION NUMBER: 93323652 MEDLINE
DOCUMENT NUMBER: 93323652 PubMed ID: 8101284
TITLE: Transdermal nicotine patch and potentiation of haloperidol in Tourette's syndrome.
AUTHOR: Silver A A; Sanberg P R
SOURCE: LANCET, (1993 Jul 17) 342 (8864) 182.
Journal code: L0S; 2985213R. ISSN: 0140-6736.
PUB. COUNTRY: ENGLAND: United Kingdom
Letter
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199308
ENTRY DATE: Entered STN: 19930826
Last Updated on STN: 19950206
Entered Medline: 19930817

L207 ANSWER 17 OF 61 MEDLINE
ACCESSION NUMBER: 94015150 MEDLINE
DOCUMENT NUMBER: 94015150 PubMed ID: 8410063
TITLE: Effects of smoking in patients with early-onset Parkinson's disease.
AUTHOR: Ishikawa A; Miyatake T
CORPORATE SOURCE: Department of Neurology, Brain Research Institute, Niigata University, Japan.
SOURCE: JOURNAL OF THE NEUROLOGICAL SCIENCES, (1993 Jul) 117 (1-2) 28-32.
Journal code: JBJ; 0375403. ISSN: 0022-510X.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199311
ENTRY DATE: Entered STN: 19940117
Last Updated on STN: 19940117
Entered Medline: 19931101

AB Smoking a cigarette relieved symptoms in 6 patients with early-onset Parkinson's disease. In these patients smoking reduced tremor, rigidity, bradykinesia, and gait disturbance including frozen gait. These effects lasted for about 10-30 min, and relieved parkinsonian symptoms in the off-period. Nicotine chewing gum had a lesser effect. Nicotine is thought to activate the nigrostriatal dopaminergic pathway and increase the release of dopamine in the striatum, and this can explain the effects of smoking in these patients.

L207 ANSWER 18 OF 61 MEDLINE
ACCESSION NUMBER: 92160997 MEDLINE
DOCUMENT NUMBER: 92160997 PubMed ID: 1599541
TITLE: Nicotine gum in Tourette's disorder.
COMMENT: Comment on: Am J Psychiatry. 1991 Jun;148(6):793-4
AUTHOR: Rickards E H
SOURCE: AMERICAN JOURNAL OF PSYCHIATRY, (1992 Mar) 149 (3) 417; discussion 418.
Journal code: 3VG; 0370512. ISSN: 0002-953X.
PUB. COUNTRY: United States
Commentary
Letter
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199203
ENTRY DATE: Entered STN: 19920410
Last Updated on STN: 19920410
Entered Medline: 19920324

L207 ANSWER 19 OF 61 MEDLINE
ACCESSION NUMBER: 92353275 MEDLINE
DOCUMENT NUMBER: 92353275 PubMed ID: 1643197
TITLE: The effects of nicotine plus haloperidol compared to nicotine only and placebo nicotine only in reducing tic severity and frequency in Tourette's disorder.
AUTHOR: McConville B J; Sanberg P R; Fogelson M H; King J; Cirino P; Parker K W; Norman A B
CORPORATE SOURCE: Department of Psychiatry, University of Cincinnati College of Medicine, Ohio 45267-0559.
SOURCE: BIOLOGICAL PSYCHIATRY, (1992 Apr 15) 31 (8) 832-40.
Journal code: A3S; 0213264. ISSN: 0006-3223.
PUB. COUNTRY: United States
(CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199209
ENTRY DATE: Entered STN: 19920925
Last Updated on STN: 19920925
Entered Medline: 19920909

AB We studied the effects of chewing nicotine gum on tic frequency and severity in 10 patients with Tourette's disorder (TD) on haloperidol, versus 9 untreated TD patients; placebo gum was administered to 5 of these untreated patients. Videotapes of patients during a 2-hr period of 30 min baseline, 30 min gum chewing, and two 30-min postgum-chewing periods were utilized. For those TD patients on haloperidol, significant reductions occurred in tic frequency and severity during the gum-chewing and the two postgum-chewing periods. Nicotine gum alone caused a decrease in tic

frequency only during gum-chewing and one postgum-chewing period, while placebo gum showed no effect. In this study, nicotine markedly potentiated haloperidol effects in treating TD, and showed lesser effects on TD when used alone.

L207 ANSWER 20 OF 61 MEDLINE
ACCESSION NUMBER: 66142869 MEDLINE
DOCUMENT NUMBER: 66142869 PubMed ID: 5937635
TITLE: Effect of adrenaline, noradrenaline, atropine, and nicotine on some types of human tremor.
AUTHOR: Marshall J; Schnieden H
SOURCE: JOURNAL OF NEUROLOGY, NEUROSURGERY AND PSYCHIATRY, (1966 Jun) 29 (3) 214-8.
Journal code: JBB; 2985191R. ISSN: 0022-3050.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 196608
ENTRY DATE: Entered STN: 19900101
Last Updated on STN: 19900101
Entered Medline: 19660829

L207 ANSWER 21 OF 61 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1
ACCESSION NUMBER: 2001:167807 CAPLUS
DOCUMENT NUMBER: 134:202708
TITLE: Use of nicotine or derivatives thereof in a medicine for treating neurological diseases, in particular Parkinson disease
INVENTOR(S): Cesaro, Pierre; Villafane, Gabriel
PATENT ASSIGNEE(S): Assistance Publique - Hopitaux de Paris, Fr.
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001015696	A1	20010308	WO 2000-FR2428	20000901
W: CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
FR 2798065	A1	20010309	FR 1999-11029	19990902

PRIORITY APPLN. INFO.: FR 1999-11029 A 19990902
AB The invention concerns the use of nicotine or a deriv. thereof for making a medicine for continuous or gradual administration of 0.2 to 5 mg daily per kilo of body wt. to a human, the medicine being administered simultaneously with L-DOPA in doses at least 30% less than efficacious doses when administered alone.
IT **54-11-5**, Nicotine **54-11-5D**, Nicotine, derivs.
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(nicotine or derivs. in combination with L-DOPA for treating neurol. diseases, esp. **Parkinson** disease)
REFERENCE COUNT: 3
REFERENCE(S):
(1) Balfour, D; PHARMACOLOGY AND THERAPEUTICS 1996, V72(1), P51 CAPLUS
(2) Domino, E; EXPERIMENTAL NEUROLOGY 1999, V158, P414 CAPLUS
(3) Lippiello, P; US 5232933 A 1993 CAPLUS

L207 ANSWER 22 OF 61 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 3
ACCESSION NUMBER: 2000:314974 CAPLUS
DOCUMENT NUMBER: 132:329942
TITLE: Use of nicotine plasters for treatment of Parkinson's disease
INVENTOR(S): Brosig, Stefan
PATENT ASSIGNEE(S): Germany
SOURCE: Ger. Offen., 2 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19850790	A1	20000511	DE 1998-19850790	19981104

AB A nicotine plaster attached to the skin produces a nicotine concn. in the body which changes relatively little over time and increases the activity of dopamine-producing nerve cells in the mesolimbic system. As a result of the prodn. of dopamine locally in the brain, external administration of dopamine for treatment of parkinsonism can be reduced or even omitted.
IT **54-11-5**, Nicotine
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(use of nicotine plasters for treatment of **Parkinson**'s disease)

L207 ANSWER 23 OF 61 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 4
ACCESSION NUMBER: 1998:553177 CAPLUS
DOCUMENT NUMBER: 129:310755
TITLE: Effects of nicotine on 1-methyl-4-phenyl-1,2,5,6-tetrahydropyridine-induced depression of striatal dopamine content and spontaneous locomotor activity in C57 black mice
AUTHOR(S): Gao, Z. G.; Cui, W. Y.; Zhang, H. T.; Liu, C. G.
CORPORATE SOURCE: Institute of Pharmacology and Toxicology, Academy of Military Medical Sciences, Beijing, 100850, Peop. Rep. China
SOURCE: Pharmacol. Res. (1998), 38(2), 101-106
CODEN: PHMREP; ISSN: 1043-6618
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The present study examd. the effects of nicotine on the levels of dopamine and its metabolite 3,4-dihydroxy-phenylacetic acid (DOPAC) in the striatum and on spontaneous locomotor activity of C57 black mice that had been treated with the neurotoxin 1-methyl-4-phenyl-1,2,5,6-tetrahydropyridine (MPTP). The levels of dopamine and DOPAC in the striatum were significantly reduced 10 days after two injections of MPTP (40 mg kg-1, i.p., 24 h apart) in mice. Chronic treatment of nicotine (2.0 mg kg-1, s.c., four injections per day) did not influence the striatal content of dopamine and DOPAC, but it significantly antagonized MPTP-induced depression of dopamine. However, the chronic nicotine treatment did not significantly affect MPTP-induced depression of DOPAC. It was demonstrated that the lethal effect of MPTP was also partly protected by the chronic nicotine treatment. The chronic nicotine treatment also significantly protected MPTP-depressed spontaneous locomotor activity in mice. The results suggest that both MPTP-depressed behavior and MPTP-induced striatal dopamine depletion in C57 black mice are partly protected by chronic nicotine treatment. The present results afford some support for a therapeutic action of nicotine in this parkinsonian animal model. (c) 1998 The Italian Pharmacological Society.

IT **54-11-5**, Nicotine
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(protective effects of nicotine on methylphenyltetrahydropyridine-induced depression of striatal dopamine content and spontaneous locomotor activity in C57 black mice in relation to **parkinsonism** treatment)

L207 ANSWER 24 OF 61 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 8
ACCESSION NUMBER: 1997:28024 CAPLUS
DOCUMENT NUMBER: 126:135463
TITLE: Transdermal nicotine for Tourette's syndrome
AUTHOR(S): Shytle, R. Doug; Silver, Archie A.; Philipp, Mary Katherine; McConville, Brian J.; Sanberg, Paul R.
CORPORATE SOURCE: Dep. Surgery, Univ. South Florida, Tampa, FL, 33612-4799, USA
SOURCE: Drug Dev. Res. (1996), 38(3-4), 290-298
CODEN: DDREDK; ISSN: 0272-4391
PUBLISHER: Wiley-Liss
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB The present review, with 50 refs., evaluates the therapeutic response to the transdermal nicotine patch (TNP) in Tourette's syndrome (TS) patients. Twenty TS patients (17 children and adolescents, 3 adults), in 18 of whom the symptoms were not controlled with neuroleptics and 2 of whom were free of medication, were followed for various lengths of time following the application of two TPs (each 7 mg/24 h). While there was a broad range in individual response, it was detd. that each application of a single TNP produced a significant redn. in Yale Global Tic Severity Scale mean scores for an av. duration of approx. 1 to 2 wk post-application. Individual case reports are discussed as well as the possible therapeutic mechanisms of transdermal nicotine in reducing the symptoms of TS. Although our data should be viewed as preliminary until controlled studies are completed, the present open-trial findings suggest that transdermal nicotine is an effective adjunct to neuroleptic therapy of TS.
IT **54-11-5**, Nicotine
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(transdermal nicotine for treatment of **Tourette**'s syndrome in humans)

L207 ANSWER 25 OF 61 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:703763 CAPLUS
DOCUMENT NUMBER: 134:187706
TITLE: Nicotinic therapeutics for Tourette syndrome and other neuropsychiatric disorders: From laboratory to clinic
AUTHOR(S): Shytle, R. Doug; Silver, Archie A.; Newman, Mary B.; Sanberg, Paul R.
CORPORATE SOURCE: Departments of Psychiatry and Behavioral Medicine, College of Medicine, University of South Florida, Tampa, FL, USA
SOURCE: Cent. Nerv. Syst. Dis. (2000), 431-440. Editor(s): Emerich, Dwaine F.; Dean, Reginald L., III. Humana Press Inc.: Totowa, N. J.
CODEN: 69ALPH
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review with 62 refs.
IT **54-11-5**, Nicotine
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(nicotinic therapeutics for **Tourette** syndrome and other neuropsychiatric disorders: from lab. to clinic)

REFERENCE COUNT: 63
REFERENCE(S): (1) Acri, J; Psychopharmacology 1994, V114, P369 CAPLUS
(3) Ahtee, L; Br J Pharmacol 1978, V62, P213 CAPLUS
(4) Arendash, G; Brain Res 1995, V674, P252 CAPLUS
(5) Arendash, G; Pharmacol Biochem Behav 1995, V52, P517 CAPLUS
(7) Arneric, S; J Pharmacol Exp Ther 1994, V270, P310 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L207 ANSWER 26 OF 61 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:595531 CAPLUS
DOCUMENT NUMBER: 134:36585
TITLE: Nicotinic treatment for degenerative neuropsychiatric disorders such as Alzheimer's disease and Parkinson's disease
AUTHOR(S): Rusted, Jennifer M.; Newhouse, Paul A.; Levin, Edward D.
CORPORATE SOURCE: Laboratory of Experimental Psychology, University of Sussex, Brighton, UK
SOURCE: Behav. Brain Res. (2000), 113(1,2), 121-129
CODEN: BBREDI; ISSN: 0166-4328
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 92 refs. Nicotinic systems play an important role in the neural basis of working memory and attention. Recent progress in understanding of the structure, function, and distribution of central nervous system (CNS) nicotinic receptors and their pharmacol. has opened up new possibilities for novel CNS therapeutics with nicotinic agents. In this paper, we review the theor. justification and the exptl. evidence supporting these developments. We focus on the applications of nicotinic agonists in CNS disorders that are degenerative in nature, namely Parkinson's disease and Alzheimer's disease. We suggest that there is considerable potential for therapeutic applications in the near future. Clin., two major issues remain: (a) the selectivity of effects, i.e., developing compds. which are selective in producing improvement in cognition, motor function, attention, or pain without significant side-effects; and (b) the realistic likelihood of long-term improvements in everyday functioning in people who have degenerative diseases.
IT **54-11-5**, Nicotine
RL: BPR (Biological process); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(nicotinic treatment for Alzheimer's disease and **Parkinson**'s disease)
REFERENCE COUNT: 92
REFERENCE(S): (1) Arendash, G; Brain Res 1995, V674, P252 CAPLUS
(2) Arneric, S; CNS Drugs Rev 1995, V1, P1 CAPLUS
(4) Aubert, I; J Neurochem 1992, V58, P529 CAPLUS
(5) Benwell, M; J Neurochem 1988, V50, P1243 CAPLUS
(6) Buccafusco, J; Psychopharmacology 1995, V120, P256 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L207 ANSWER 27 OF 61 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:71712 CAPLUS
DOCUMENT NUMBER: 126:166386
TITLE: Interactions between a novel cholinergic ion channel agonist, SIB-1765F, and L-DOPA in the reserpine model of Parkinson's disease in rats
AUTHOR(S): Menzaghi, Frederique; Whelan, Kevin T.; Risbrough, Victoria B.; Rao, Tadimeti S.; Lloyd, G. Kenneth

CORPORATE SOURCE: SIBIA Neurosci., Inc., La Jolla, CA, USA
SOURCE: J. Pharmacol. Exp. Ther. (1997), 280(1), 393-401
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB SIB-1765F was tested for its efficacy in attenuating reserpine-induced hypolocomotion in rats. SIB-1765F was administered alone or in combination with L-DOPA and its effects were compared with those of nicotine, d-amphetamine and amantadine in the same conditions. Consistent with previous reports, reserpine-induced hypolocomotion was reversed by L-DOPA (plus benserazide), d-amphetamine and amantadine in a dose-dependent manner, and the effect of L-DOPA in reserpine-treated rats was potentiated by amantadine. SIB-1765F also increased the locomotor activity of reserpine-treated rats and potentiated the effect of L-DOPA on reserpine-induced hypolocomotion. The onset of potentiation of the effect of L-DOPA by SIB-1765F was rapid (<5 min) compared to that by amantadine (>105 min). Nicotine did not attenuate reserpine-induced hypolocomotion nor did it affect the action of L-DOPA on reserpine-treated rats. Biochem. anal. of levels of dopamine and its metabolites, dihydroxyphenylacetic and homovanillic acids, in the striatum and olfactory tubercles indicated that, in contrast to amphetamine, SIB-1765F did not inhibit dopamine reuptake. The effect of SIB-1765F in reserpine-treated rats was attenuated by .alpha.-methyl-p-tyrosine, implying that SIB-1765F acts by releasing dopamine from both reserpine-insensitive and reserpine-sensitive pools. Nicotinic acetylcholine receptor agonists may offer a new therapeutic approach to the symptomatic treatment of the motor deficits in patients with Parkinson's disease.

IT **54-11-5**, Nicotine
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(SIB-1765F and dopa effect on locomotor behavior in model of **parkinsonism** in comparison with those of)

L207 ANSWER 28 OF 61 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:477167 CAPLUS
DOCUMENT NUMBER: 129:254160
TITLE: Nicotine as a therapeutic adjunct for Tourette's syndrome
AUTHOR(S): Sanberg, P. R.; Silver, A. A.; Mcconville, J.; Philipp, M. K.; Gonzalez, L.; Cahill, D. W.; Shytle, R. D.
CORPORATE SOURCE: Tampa, FL, USA
SOURCE: Immun. Environ. (1997), 10(Nicotine As A Therapeutic Agent), 35-41
CODEN: IMENFY; ISSN: 0940-1547
PUBLISHER: Gustav Fischer Verlag
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 40 refs.

IT **54-11-5**, Nicotine
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(nicotine as a therapeutic adjunct for **Tourette**'s syndrome in humans)

L207 ANSWER 29 OF 61 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 6
ACCESSION NUMBER: 96158477 EMBASE
DOCUMENT NUMBER: 1996158477
TITLE: Pharmacology of nicotine: Addiction and therapeutics.
AUTHOR: Benowitz N.L.

CORPORATE SOURCE: Clinical Pharmacology Unit, Medical Service, San Francisco General Hosp. Med. Ct.,San Francisco, CA 94143-1220, United States
SOURCE: Annual Review of Pharmacology and Toxicology, (1996) 36/-(597-613).
ISSN: 0066-4251 CODEN: ARPTDI
COUNTRY: United States
DOCUMENT TYPE: Journal; **General Review**
FILE SEGMENT: 008 Neurology and Neurosurgery
020 Gerontology and Geriatrics
032 Psychiatry
040 Drug Dependence, Alcohol Abuse and Alcoholism
046 Environmental Health and Pollution Control
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Nicotine maintains tobacco addiction and has therapeutic utility to aid smoking cessation and possibly to treat other medical diseases. Nicotine acts on nicotinic cholinergic receptors, which demonstrate diversity in subunit structure, function, and distribution within the nervous system, presumably mediating the complex actions of nicotine described in tobacco users. The effects of nicotine in people are influenced by the rate and route of dosing and by the development of tolerance. The metabolism of nicotine is now well characterized in humans. A few individuals with deficient C-oxidation of nicotine, unusually slow metabolism of nicotine, and little generation of cotinine have been described. Nicotine affects most organ systems in the body, although its contribution to smoking-related disease is still unclear. Nicotine as a medication is currently available as a gum, a transdermal delivery device, and a nasal spray, all of which are used for smoking cessation. Nicotine is also being investigated for therapy of ulcerative colitis, Alzheimer's disease, Parkinson's disease, Tourette's syndrome, sleep apnea, and attention deficit disorder.

L207 ANSWER 30 OF 61 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 9
ACCESSION NUMBER: 95267093 EMBASE
DOCUMENT NUMBER: 1995267093
TITLE: [Nicotine - From stimulant to potential therapeutic agent?].
NICOTIN - VOM GENUSSMITTEL ZUM ARZNEISTOFF?.
AUTHOR: Muller C.E.
CORPORATE SOURCE: Inst. Pharmazie/Lebensmittelchemie, Am Hubland,97074 Wurzburg, Germany
SOURCE: Deutsche Apotheker Zeitung, (1995) 135/36 (17-32).
ISSN: 0011-9857 CODEN: DAZEA2
COUNTRY: Germany
DOCUMENT TYPE: Journal; **General Review**
FILE SEGMENT: 037 Drug Literature Index
LANGUAGE: German
SUMMARY LANGUAGE: German

L207 ANSWER 31 OF 61 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999191698 EMBASE
TITLE: The therapeutic potential of nicotine and nicotinic agonists for weight control.
AUTHOR: Gurwitz D.
CORPORATE SOURCE: D. Gurwitz, Natl. Lab. Genet. Israeli Population, Sackler Faculty of Medicine, Tel-Aviv University, Tel-Aviv 69978, Israel. gurwitz@post.tau.ac.il
SOURCE: Expert Opinion on Investigational Drugs, (1999) 8/6 (747-760).
Refs: 157

ISSN: 1354-3784 CODEN: EOIDER
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; **General Review**
FILE SEGMENT: 017 Public Health, Social Medicine and Epidemiology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Transdermal nicotine patches have been successfully introduced as a safe and powerful aid to smoking cessation; this has contributed to the rising interest in additional therapeutic applications for nicotine and synthetic nicotinic agonists. Nicotine and nicotinic agonists may have a therapeutic potential for a variety of disorders, including Alzheimer's and Parkinson's diseases, depression, attention deficit disorder, Tourette's syndrome and ulcerative colitis. These interests are partially fuelled by the urgent need of the tobacco industry to find new niches for nicotine in a world bound eventually to retire from cigarette smoking. At the same time, there is an increased interest in developing drugs for fighting obesity, a growing affliction of industrialised nations. This review presents data on the potential of nicotine, and in particular synthetic nicotinic agonists, for controlling body weight. Nicotinic agonists may become relatively safe, effective and inexpensive alternatives for several optional drugs currently being developed for treating human obesity, including .beta.-3-adrenergic agonists, leptin and its agonists, and neuropeptide Y antagonists.

L207 ANSWER 32 OF 61 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000399745 EMBASE
TITLE: Nicotinic cholinergic receptor deficits in Alzheimer's disease: Where's the smoke?.
AUTHOR: Pauly J.R.
CORPORATE SOURCE: J.R. Pauly, Division of Pharmaceutical Sciences, College of Pharmacy, University of Kentucky, Lexington, KY 40536-0082, United States. jpauly@pop.uky.edu
SOURCE: Journal of Alzheimer's Disease, (1999) 1/4-5 (221-230).
Refs: 55
ISSN: 1387-2877 CODEN: JADIF
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; **General Review**
FILE SEGMENT: 008 Neurology and Neurosurgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Receptor binding studies have uniformly found a significant reduction in the density of neuronal nicotinic cholinergic receptors in postmortem tissue obtained from Alzheimer's Disease (AD) patients. Nicotine is widely recognized as an pharmacological agent that facilitates cognitive performance in human smokers as well as preclinical models utilizing rodents or non-human primates. Furthermore, epidemiological studies have consistently shown that the incidence of neurodegenerative diseases such as AD and Parkinson's Disease is lower in cigarette smokers than age-matched controls. These findings have prompted speculation that brain nicotinic receptors could be important therapeutic targets for Alzheimer's Disease. However, many questions remain with regard to the specificity and significance of the findings that have been reported with brain nicotinic receptors and AD. Few studies have controlled for the potential influence of cigarette smoking, which increases the density of nicotinic receptors in human smokers. Questions also remain concerning alterations in individual nicotinic receptors subtypes as well as the regional variability of the deficits previously reported in AD. Therefore, although the findings related to nicotinic receptors and AD to this date are intriguing, they appear to have raised more questions than they have answered.

L207 ANSWER 33 OF 61 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999076783 EMBASE
TITLE: Clinical experience with transdermal nicotine patch in Tourette syndrome.
AUTHOR: Silver A.A.; Shytle R.D.; Sanberg P.R.
CORPORATE SOURCE: Dr. A.A. Silver, Institute for Research in Psychiatry, College of Medicine, University of South Florida, Tampa, FL, United States
SOURCE: CNS Spectrums, (1999) 4/2 (68-76).
Refs: 24
ISSN: 1092-8529 CODEN: CNSPFH
COUNTRY: United States
DOCUMENT TYPE: Journal; **General Review**
FILE SEGMENT: 008 Neurology and Neurosurgery
032 Psychiatry
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Stemming from the finding that nicotine potentiates haloperidol-induced catalepsy in rats, nicotine in the form of nicotine gum and as transdermal nicotine patch (TNP) has been used in open-label studies to obtund motor and vocal tics of children (age.gtoreq.8 years, weight.gtoreq.25 kg), adolescents, and adults. Reduction of tics was seen during chewing of nicotine gum; the improvement lasted no longer than 1 hour after chewing. With a TNP in subjects who were not responding well to a variety of dopamine blockers, with some also receiving clonidine or a variety of selective serotonin reuptake inhibitors, motor and vocal tics were obtunded 45% over baseline in 85% of 35 subjects within 30 minutes to 3 hours after TNP application. Moreover, the relief of symptoms with a single 7-mg TNP, remaining on the skin for 24 hours, persisted for a variable period of time ranging from 1 to 120 days with an average of 10.+-.2 days. Application of a second TNP for 24 hours when symptoms began to return resulted in a similar reduction in tic severity and frequency, which persisted an average of 13.+-.3 days. Nicotine alone, without D2 blockers, was successful in reducing premonitory urges to tic. After follow-up of 3 to 5 years, 19 of 35 patients continued to use the TNP in gradually decreasing frequency and with gradual reduction in dose of D2 blockers. However, 16 patients (45%), as they grew into middle adolescence, discontinued use of the TNP, stating that they objected to the nausea induced by the patch. There was no evidence of habituation to nicotine. Side effects were not life threatening; the most disturbing side effect was nausea, appearing 1 to 4 hours after the application of the patch and lasting 1 to 3 hours. There was no change in blood pressure; pulse rate increased from 5 to 10% within 3 hours but returned to baseline after 24 hours. Unsolved problems using TNP are mentioned and a putative mechanism for nicotine effectiveness in Tourette syndrome is briefly discussed.

L207 ANSWER 34 OF 61 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998141361 EMBASE
TITLE: Nicotine: Abused substance and therapeutic agent.
AUTHOR: Le Houezec J.
CORPORATE SOURCE: Dr. J. Le Houezec, CNRS URA 1957, Hopital de la Salpetriere, 47, Bouleveard de l'Hopital, F-75651 Paris Cedex 13, France. jlehouez@ext.jussieu.fr
SOURCE: Journal of Psychiatry and Neuroscience, (1998) 23/2 (95-108).
Refs: 145
ISSN: 1180-4882 CODEN: JPNEEF
COUNTRY: Canada
DOCUMENT TYPE: Journal; **General Review**
FILE SEGMENT: 008 Neurology and Neurosurgery

030 Pharmacology
032 Psychiatry
037 Drug Literature Index
040 Drug Dependence, Alcohol Abuse and Alcoholism
LANGUAGE: English
SUMMARY LANGUAGE: English; French
AB Tobacco dependence is a complex phenomenon that is not fully understood. Nicotine is the main alkaloid in tobacco and the addictive compound of tobacco. It can improve both mood and cognitive functioning, these positive effects are strong reinforcements for smokers and contribute to their addiction. Opposite results also have been reported, however, and the effects of nicotine remain controversial. Recent epidemiological and empirical studies have indicated that smoking or nicotine or both may have protective effects against certain diseases. These findings have suggested that nicotine may be used as a therapeutic agent. However, because a variety of nicotinic cholinergic receptors are present in the brain, new agonist compounds may prove to be more effective than nicotine for therapeutic purposes. Studies are reviewed and the suggestion made that nicotine may prove useful as a tool to help us understand normal and pathological brain functioning.

L207 ANSWER 35 OF 61 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96031825 EMBASE
DOCUMENT NUMBER: 1996031825
TITLE: Society for research on nicotine and tobacco.
AUTHOR: Perkins K.A.; Benowitz N.; Henningfield J.; Newhouse P.; Pomerleau O.; Swan G.
CORPORATE SOURCE: WPIC, Univ. Pittsburgh School of Medicine, 3811 O'Hara Street,Pittsburgh, PA 15213, United States
SOURCE: Addiction, (1996) 91/1 (129-137).
ISSN: 0965-2140 CODEN: ADICE5
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 017 Public Health, Social Medicine and Epidemiology
036 Health Policy, Economics and Management
037 Drug Literature Index
040 Drug Dependence, Alcohol Abuse and Alcoholism
LANGUAGE: English
SUMMARY LANGUAGE: English; French; Spanish
AB The proceedings of the inaugural scientific meeting of the Society for Research on Nicotine and Tobacco (SRNT) are summarized. The primary objective of the meeting was to foster the exchange of information on the effects of nicotine and tobacco use, as well as factors which influence their use, drawing from biological, behavioral and social sciences. Much of this research can be viewed as a tale of 'two' drugs - nicotine as a key to an important public health problem, and nicotine as a classical tool of physiological and pharmacological research. A historical overview of research on 'both' drugs is provided first. Public policy alternatives for reducing the prevalence of tobacco use have been derived in part from basic and clinical research results and are briefly outlined. Evidence for genetic determinants on nicotine use and effects is presented using data from twin studies and from molecular genetic research with humans and animals. Consistent with this research, there is evidence of individual differences in pharmacokinetics and effects of nicotine, which could account for differences in smoking behavior and nicotine dependence. Finally, recent developments in the therapeutic uses of nicotine and novel nicotinic agonists with schizophrenia, Alzheimer's disease, Parkinson's disease, Tourette's syndrome and ulcerative colitis are presented. Overall, the research presented at the meeting demonstrated the vast diversity of areas of study involving nicotine and tobacco, as well as the rich opportunities for cross-communication among researchers from different disciplines.

L207 ANSWER 36 OF 61 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96012503 EMBASE
DOCUMENT NUMBER: 1996012503
TITLE: Cholinergic channel modulators as a novel therapeutic strategy for Alzheimer's disease.
AUTHOR: Arneric S.P.; Holladay M.W.; Sullivan J.P.
CORPORATE SOURCE: Neuroscience Discovery, Pharmaceutical Products Division, Abbott Laboratories,Abbott Park, IL 60064-3500, United States
SOURCE: Expert Opinion on Investigational Drugs, (1996) 5/1 (79-100).
ISSN: 1354-3784 CODEN: EOIDER
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; **General Review**
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
008 Neurology and Neurosurgery
022 Human Genetics
023 Nuclear Medicine
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Advances in the molecular biological knowledge of neuronal nicotinic acetylcholine receptors (nAChRs) have led to a growing interest by the pharmaceutical industry in the development of novel compounds that selectively modulate nAChR function. The ability of (-)-nicotine, an activator of nAChRs, to enhance attentional aspects of cognition in animals and humans, to exert neuroprotective and anxiolytic-like effects, and presumably to mediate the negative correlation between smoking and Alzheimer's (and Parkinson's) Disease, has focused interest on the potential therapeutic utility of modulators of nAChR function for treatment of some of the deficits associated with these progressive, neurodegenerative conditions. Numerous compounds are known which activate nAChRs and which might serve as lead compounds toward the development of such agents. The pharmacologic diversity of neuronal nAChR subtypes suggests the possibility of developing selective compounds which would have more favourable side-effect profiles than existing agents. This broader class of agents, collectively called cholinergic channel modulators (ChCMs), is anticipated to encompass compounds which would have more favourable side-effect profiles than existing agents, which generally exhibit low selectivity. This selectivity may be achieved by preferentially activating some subtypes of nAChRs (i.e., Cholinergic Channel Activators, ChCAs) or inhibiting the function of other subtypes (Cholinergic Channel inhibitors, ChCIs). An overview of the biology of nAChRs and the rationale for the use of ChcMs for the treatment of dementia related to neurodegenerative diseases are presented, followed by a discussion of lead compounds and compounds under consideration for clinical evaluation.

L207 ANSWER 37 OF 61 DRUGU COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2001-19342 DRUGU P
TITLE: Dose-related neuroprotective effects of chronic nicotine in 6-hydroxydopamine treated rats, and loss of neuroprotection in alpha4 nicotinic receptor subunit knockout mice.
AUTHOR: Ryan R E; Ross S A; Drago J; Loiacono R E
CORPORATE SOURCE: Univ.Monash
LOCATION: Melbourne, Austr.
SOURCE: Br.J.Pharmacol. (132, No. 8, 1650-56, 2001) 2 Fig. 49 Ref.
CODEN: BJPCBM ISSN: 0007-1188
AVAIL. OF DOC.: Department of Pharmaceutical Biology and Pharmacology, Victorian College of Pharmacy, Monash University, Parkville, Victoria 3052, Australia. (e-mail:

rebecca.ryan@vcp.monash.edu.au).
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB Chronic administration of s.c. (-)-nicotine di-d-tartrate produced dose-dependent neuroprotective effect on intrastriatal 6-hydroxydopamine (6-OHDA) (both Research-Biochem.)-induced loss of striatal dopaminergic nerve terminals in rats. Acute nicotine treatment provided protection against i.p. methamphetamine-induced neurodegeneration in wild-type (WT) mice. However, nicotine failed to attenuate methamphetamine-induced loss of dopaminergic terminals in alpha4 nicotinic receptor (nAChR) subunit knockout mice. Results suggest that nicotine is capable of protecting dopaminergic neurons against Parkinsonian-like neurodegeneration in vivo.

L207 ANSWER 38 OF 61 DRUGU COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2001-15899 DRUGU P
TITLE: Nicotine, but not cotinine, partially protects dopaminergic neurons against MPTP-induced degeneration in mice.
AUTHOR: Parain K; Marchand V; Dumery B; Hirsch E
LOCATION: Paris, Fr.
SOURCE: Brain Res. (890, No. 2, 347-50, 2001) 2 Fig. 19 Ref.
CODEN: BRREAP ISSN: 0006-8993
AVAIL. OF DOC.: INSERM U289, Hopital de la Salpetriere, 47 Bd de l'Hopital, 75651 Paris Cedex 13 France. (E.H.). (e-mail: Hirsch@ccr.jussieu.fr).
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB I.p. nicotine, but not cotinine (both Sigma-Aldrich), slightly protected dopaminergic neurons against MPTP intoxication. MPTP intoxication induced a loss of dopaminergic perikarya in the substantia nigra and a decrease in dopaminergic fibers in the striatum. As cotinine transfer to the brain is less efficient than that of nicotine, a neuroprotective action of this compound might be observed at higher concentrations. Thus, further studies are needed to determine whether other compounds present in cigarette smoke can protect dopaminergic neurons against degeneration in Parkinson's disease.

L207 ANSWER 39 OF 61 DRUGU COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1998-07836 DRUGU T
TITLE: Gilles de la Tourette syndrome. Effects of nicotine, alcohol and marijuana on clinical symptoms.
AUTHOR: Mueller Vahl K R; Kolbe H; Dengler R
LOCATION: Hannover, Ger.
SOURCE: Nervenarzt (68, No. 12, 985-89, 1997) 43 Ref.
CODEN: NERVAF ISSN: 0028-2804
AVAIL. OF DOC.: Neurologische Klinik mit Klinischer Neurophysiologie, Medizinische Hochschule Hannover, Carl-Neuberg Strasse 1, D-30623 Hannover, Germany.
LANGUAGE: German
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB When 47 patients with Gilles de la Tourette syndrome (GTS) were asked about the effects of smoking, alcohol and marijuana on their symptoms, only a few of the smokers said their symptoms were reduced by nicotine, whereas many of the subjects who regularly drank alcohol reported that it lessened their symptoms. Marijuana was also said to reduce symptoms in the majority of users.

L207 ANSWER 40 OF 61 DRUGU COPYRIGHT 2002 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1997-19561 DRUGU P B
TITLE: Nicotine protection in experimental parkinsonism: a role for neurotrophic factors.
AUTHOR: Riva M A; Begni B; Vaglini F; Racagni G; Corsini G U; Maggio R
CORPORATE SOURCE: Univ.Milan; Univ.Pisa
LOCATION: Milan; Pisa, It.
SOURCE: Pharmacol.Res. (35, Suppl., 34, 1997)
CODEN: PHMREP ISSN: 1043-6618
AVAIL. OF DOC.: Center for Neuropharmacology, University of Milan, Italy.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB (-)-Nicotine showed protective effects in rat and mouse models of parkinsonism (the diethyldithiocarbamate (DCC)-induced enhancement of MPTP toxicity in rats and the methamphetamine-induced neurotoxicity, respectively). (-)-Nicotine increased the gene expression of basic fibroblast growth factor-2 and, to a lesser extent, brain-derived neurotrophic factor in the striatum, but not in other brain regions. The results suggest that the protective effect of (-)-nicotine in parkinsonism amy be due to an increase in the production of neurotrophic factors. (conference abstract).

L207 ANSWER 41 OF 61 DRUGU COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1997-04470 DRUGU P T S
TITLE: Pharmacology and nicotine and its therapeutic use in smoking cessation and neurodegenerative disorders.
AUTHOR: Balfour D J K; Fagerstroem K O
CORPORATE SOURCE: Univ.Dundee, Pharmacia; Upjohn
LOCATION: Dundee, U.K.; Helsingborg, Swed.
SOURCE: Pharmacol.Ther. (72, No. 1, 51-81, 1996) 2 Fig. 6 Tab. 262 Ref.
CODEN: PHTHDT ISSN: 0163-7258
AVAIL. OF DOC.: Neuroscience Research Institute, Department of Pharmacology, University of Dundee Medical School, Ninewells Hospital, Dundee, Scotland.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB The pharmacology of nicotine and its therapeutic use in smoking cessation and neurodegenerative disorders such as Parkinson's disease and Alzheimer's disease are reviewed. The neuropharmacological properties of nicotine, its effects on animal behavior, on learning and memory, the pharmacological preparations used to in smoking cessation, its pharmacokinetics, clinical efficacy and side-effects are discussed. Amphetamine, cocaine, mecamylamine and pentetrazol are also mentioned.

L207 ANSWER 42 OF 61 DRUGU COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1996-32211 DRUGU P
TITLE: Effects of acute nicotine administration on parkinsonain disability and dyskinesia in MPTP-treated common marmosets.
AUTHOR: Banerji T; Pearce R K B; Desai N B; Jackson M J; Jenner P; Marsden C D
CORPORATE SOURCE: Univ.London
LOCATION: London, U.K.
SOURCE: Br.J.Pharmacol. (118, Proc.Suppl., 38P, 1996) 1 Fig. 3 Ref.
CODEN: BJPCBM ISSN: 0007-1188
AVAIL. OF DOC.: Neurodegenerative Diseases Research Centre, Pharmacology Group, King's College, London SW3 6LX, England.
LANGUAGE: English
DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB The effects of acute s.c. nicotine administration on motor disability and dyskinesia induced by pretreatment with MPTP or MPTP and p.o. L-DOPA were determined in common marmosets. The results showed reduced disability scores in L-DOPA-primed animals after nicotine, but no significant positive effect of acute nicotine administration on dyskinesia or locomotor activity in the animal model. The delay of onset of L-DOPA's actions by nicotine suggest either an impairment of L-DOPA absorption or an inhibitory effect of nicotine on the action of L-DOPA in the brain. (conference abstract).

L207 ANSWER 43 OF 61 DRUGU COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1997-04230 DRUGU P
TITLE: Nicotine protects from experimental parkinsonism.
AUTHOR: Corsini G U; Vaglini F; Fornai F; Maggio R
CORPORATE SOURCE: Univ.Pisa-Inst.Pharmacol.
LOCATION: Pisa, It.
SOURCE: J.Neural Transm. (103, No. 10, X, 1996)
CODEN: JNTMAH ISSN: 0300-9564
AVAIL. OF DOC.: Instituto di Farmacologia, Universita di Pisa, Italy
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB The neuroprotective effect of nicotine in 2 animal models of Parkinson's disease, the diethyldithiocarbamate induced enhancement of 1-methyl-4-phenyl 1,2,3,6-tetrahydropyridine toxicity in mice and the methamphetamine induced neurotoxicity in mice and rats, were described. The results indicated an increase of neurotrophic factors as a possible mechanism by which nicotine protected from experimental parkinsonism. (conference abstract). (No EX).

L207 ANSWER 44 OF 61 DRUGU COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1995-16937 DRUGU T S
TITLE: The short-term effect of nicotine chewing gum in patients with Parkinson's disease.
AUTHOR: Clemens P; Baron J A; Coffey D; Reeves A
LOCATION: Hanover, N.H., USA
SOURCE: Psychopharmacology(Berlin) (117, No. 2, 253-56, 1995) 4 Fig. 23 Ref.
CODEN: PSCHDL ISSN: 0033-3158
AVAIL. OF DOC.: Department of Medicine, Darthmouth-Hitchkock Medical Center, Hanover, NH 03756, U.S.A. (J.A.B.).
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB In a short-term, placebo-controlled, double-blind trial in 48 Parkinson's disease patients, nicotine polacrilex chewing gum (Nicorette) had no significant effect on Parkinsonian symptoms. Nicotine was well tolerated, but vomiting and nausea occurred in a few cases. Most of the patients were also receiving L-dopa or carbidopa. A longer-term trial may be feasible.

L207 ANSWER 45 OF 61 DRUGU COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1995-10162 DRUGU T
TITLE: Differential effects of transdermal nicotine patch on the symptoms of Tourette's syndrome.
AUTHOR: Dursun S M; Bird R; Reveley M A
CORPORATE SOURCE: Univ.Leicester
LOCATION: Leicester, U.K.
SOURCE: Br.J.Clin.Pharmacol. (39, No. 1, 100P-101P, 1995) 1 Tab. 4

Ref.
CODEN: BCPHBM ISSN: 0306-5251
AVAIL. OF DOC.: Department of Psychiatry, Faculty of Medicine, University of Leicester, Leicester LE2 7LX, England.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB 2 10 Mg transdermal nicotine patches (TNP) were applied for 2 consecutive days to 3 male non-smoking Tourette's syndrome (TS) patients (1 a drug-naive 14-yr-old and the other 2 were 44- and 18-yr-old patients refractory to haloperidol). Follow-up was 4 wk. Results demonstrated that TNP may be effective in reducing symptoms of TS (up to 4 wk) in non-smoking patients who are not satisfactorily controlled with haloperidol. Application of TNP plus haloperidol differentially affected the symptoms of TS which suggest that the nicotinic cholinoceptors may be differentially involved in the generation of the symptoms of TS. (conference abstract). (No EX).

L207 ANSWER 46 OF 61 DRUGU COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1996-33624 DRUGU P B
TITLE: Nicotine prevents MPTP experimental parkinsonism in rodents.
AUTHOR: Vaglini F; Fascetti F; Pardini C; Mancino L; Corsini G U
CORPORATE SOURCE: Univ.Pisa-Inst.Pharmacol.
LOCATION: Pisa, It.
SOURCE: J.Neural Transm. (102, No. 3, L, 1995)
CODEN: JNTMAH ISSN: 0300-9564
AVAIL. OF DOC.: Institute of Pharmacology, School of Medicine, University of Pisa, Italy.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB (-)Nicotine (1 mg/kg, s.c.) administered 3 times (90 and 30 min before and 30 min after MPTP) completely prevented both the marked depletion of striatal dopamine and the severe loss of tyrosine hydroxylase-positive pericarya in the substantia nigra pars compacta induced by combined treatment of mice with diethyldithiocarbamate + MPTP. The findings suggested that nicotine could be responsible for the reduced prevalence of Parkinson's disease among smokers. Possible mechanisms are discussed, including NMDA antagonism and nicotinic cholinergic receptor activation. (conference abstract). (No EX).

L207 ANSWER 47 OF 61 DRUGU COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1996-33588 DRUGU T S
TITLE: Nicotine and neuropsychiatric movement disorders.
AUTHOR: Erdmann R; Hoegemann D
CORPORATE SOURCE: Univ.Hanover
LOCATION: Hanover, Ger.
SOURCE: J.Neural Transm. (102, No. 3, XIII-XIV, 1995)
CODEN: JNTMAH ISSN: 0300-9564
AVAIL. OF DOC.: Department of Clinical Psychiatry and Psychotherapy, Medizinische Hochschule Hannover, Germany.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB Nicotine (NC) was found to have positive effects in patients with Tourette syndrome (TS) and possibly in tardive dyskinesia (TD) as well as neuroleptic-induced Parkinsonism (NIP), but not in idiopathic Parkinson's disease (IPD). With respect of epidemiological, electrophysiological, pathobiochemical and pathophysiological studies and the Authors' present preliminary results, a hypothetical model of the NC effects in

neuropsychiatric movement disorders suggests that acute NC administration leads to a higher activity in the frontal cortex and amelioration of the symptomatology, especially in TS. Chronic NC administration desensitizes the dopaminergic receptors in the nigro-striatal system with positive results in TS and TD, but negative results in IPD and NIP. NC is possibly helpful in the treatment of some movement disorders. (conference abstract). (No EX).

L207 ANSWER 48 OF 61 DRUGU COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1995-01775 DRUGU T
TITLE: Longlasting improvement of Tourette's syndrome with transdermal nicotine.
AUTHOR: Dursun S M; Reveley M A; Bird R; Stirton F
CORPORATE SOURCE: Univ.Leicester
LOCATION: Leicester, U.K.
SOURCE: Lancet (344, No. 8936, 1577, 1994) 1 Tab. 4 Ref.
CODEN: LANCAO ISSN: 0140-6736
AVAIL. OF DOC.: Department of Psychiatry, Robert Kilpatrick Clinical Sciences Building, University of Leicester, Faculty of Medicine, Leicester LE2 7LX, England.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB A study of 5 patients (pts) with long-lasting improvement of Tourette's syndrome with transdermal nicotine patches (TNP) is reported in a letter. All pts were neither active nor passive smokers. All but 1 pt were also receiving haloperidol (HA). TNP reduced the number of tics with no reported side-effects for up to 4 wk but not 16 wk, athough there was still a tendency towards reduction after this time period. This dose regimen may be effective in improving the tics of non-smoking pts who have not received medication and also those whose symptoms cannot be controlled with neuroleptics. TNP is effective as sole treatment or an addition to HA. TNP may induce improvement by prolonging desensitization of brain nicotinic receptors. Further research is required to determine the dose-dependent efficacy of TNP and the role of brain nicotinic receptors in Tourette's syndrome.

L207 ANSWER 49 OF 61 DRUGU COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1994-44767 DRUGU T
TITLE: Microstructural analysis of the symptoms of Tourette's syndrome and the effects of a trial use of transdermal nicotine patch.
AUTHOR: Reveley M A; Bird R; Sirton R F; Dursun S M
CORPORATE SOURCE: Univ.Leicester
LOCATION: Leicester, United Kingdom
SOURCE: J.Psychopharmacol.(Oxford) (Conf.Abstr., A30, 1994) 3 Ref.
CODEN: JOPSEQ ISSN: 0269-8811
AVAIL. OF DOC.: Department of Psychiatry, Faculty of Medicine, University of Leicester, Leicester LE2 7LX, England.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB Transdermal nicotine patches (TNP; Pharmacia) were evaluated in the treatment of 2 patients with Tourette's syndrome (TS). 1 Patient was previously untreated, the other had failed to respond to haloperidol (HP). beneficial effects were demonstrated in both patients. The results suggested that the nicotinic-cholinoceptors may be differentially involved in the generation of the symptoms of TS, alternatively TNP affected these symptoms via altering the dopaminergic and/or serotoninergic neurotransmission. (conference abstract).

L207 ANSWER 50 OF 61 DRUGU COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1993-35726 DRUGU T P
TITLE: Transdermal Nicotine Patch and Potentiation of Haloperidol in Tourette's Syndrome.
AUTHOR: Silver A A; Sanberg P R
LOCATION: Tampa, Florida, United States
SOURCE: Lancet (342, No. 8864, 182, 1993) 2 Ref.
CODEN: LANCAO ISSN: 0140-6736
AVAIL. OF DOC.: University of South Florida College of Medicine, Tampa, Florida 33612, U.S.A.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB 2 Cases of Tourette's syndrome (TS) treated with transdermal nicotine patch are reported. In 1 patient NC may have potentiated the effect of haloperidol. Prior therapy included clomipramine and perphenazine. NC improved TS symptoms in a man whose symptoms had not responded to clonidine. NC decreased tension in 2 smokers with TS who had not benefited from haloperidol therapy.

L207 ANSWER 51 OF 61 DRUGU COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1989-17141 DRUGU P T S
TITLE: Nicotine Potentiates the Effects of Haloperidol in Animals and in Patients with Tourette Syndrome.
AUTHOR: Sanberg P R; McConville J; Fogelson H M; Manderscheid P Z; Parker K W; Blythe M M
LOCATION: Cincinnati, Ohio, United States
SOURCE: Biomed.Pharmacother. (43, No. 1, 19-23, 1989) 2 Tab. 16 Ref.
CODEN: BIPHEX ISSN: 0753-3322
AVAIL. OF DOC.: Division of Neuroscience, Department of Psychiatry, University of Cincinnati College of Medicine, Cincinnati, OH 45267-0559, U.S.A. (8 authors).
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB I.p. nicotine (NT, Sigma-Chem.) in rats potentiated i.p. haloperidol (HP, Research Biochem.)-induced hypokinesia. Administration of NT chewing gum (Nicotette) in 10 children with Tourette syndrome being treated with p.o. HP produced a substantial decrease in tics and improvement of concentration and attention span. NT gum alone was without effect. The majority of children discontinued the gum due to side effects (experienced by all children) which included stomach aches, weight loss, nausea, vomiting, bitter taste and lightheadedness. NT may prove useful as adjunctive therapy in other neuroleptic-responsive disorders.

L207 ANSWER 52 OF 61 DRUGU COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1988-20810 DRUGU T P S
TITLE: Nicotine Gum and Haloperidol in Tourette's Syndrome.
AUTHOR: Sanberg P R; Fogelson H M; Manderscheid P Z; Parker K W; Norman A B; McConville B J
LOCATION: Cincinnati, Ohio, United States
SOURCE: Lancet (1988, I, No. 8585, 592) 5 Ref.
CODEN: LANCAO ISSN: 0140-6736
AVAIL. OF DOC.: Department of Psychiatry, University of Cincinnati College of Medicine, Cincinnati, Ohio 45267, U.S.A.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB 2 Cases of improvement in the symptoms of Tourette's syndrome (an extrapyramidal movement disorder) after nicotine (NC, Nicorette

chewing-gum) was added to existing haloperidol (HP) treatment are reported.Drowsiness, increased appetite and weight gain were observed with HP, and stomach ache and weight loss with NC. Methylphenidate therapy had been used previously in 1 patient. The mechanism of action whereby NC can potentiate the behavior of neuroleptics needs elucidation, although it has been shown to interact with the dopaminergic system. NC may prove useful for treating other neuroleptic-responsive disorders such as schizophrenia and Huntington's disease.

L207 ANSWER 53 OF 61 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1999-419082 [35] WPIDS
CROSS REFERENCE: 1997-525229 [45]; 1998-086592 [06]; 1998-086593 [06]; 1998-086595 [06]; 1998-286402 [20]; 1998-311923 [20]; 1998-583177 [47]; 1998-583178 [47]; 1998-609971 [49]; 1999-059765 [05]; 1999-204008 [17]; 1999-600839 [50]; 2000-037105 [03]
DOC. NO. CPI: C1999-123242
TITLE: New phosphinyl-alkanoic acid derivatives for treating glutamate-related disorders such as epilepsy, and prostatic cancer or benign hypertrophy.
DERWENT CLASS: B05
INVENTOR(S): JACKSON, P F; LI, W; MACLIN, K M; SLUSHER, B S; TAYS, K L; TSUKAMOTO, T
PATENT ASSIGNEE(S): (GUIL-N) GUILFORD PHARM INC
COUNTRY COUNT: 84
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9933847	A1	19990708	(199935)*	EN	176
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW					
AU 9920066	A	19990719	(199951)		
US 6071965	A	20000606	(200033)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9933847	A1		WO 1998-US27175	19981221
AU 9920066	A		AU 1999-20066	19981221
US 6071965	A	CIP of	US 1996-665775	19960617
		CIP of	US 1996-665776	19960617
		CIP of	US 1996-718703	19960927
		CIP of	US 1996-775586	19961231
		CIP of	US 1996-778733	19961231
		CIP of	US 1997-825997	19970404
		CIP of	US 1997-835572	19970409
		CIP of	US 1997-842360	19970424
		CIP of	US 1997-858985	19970527
		CIP of	US 1997-863624	19970527
		CIP of	US 1997-864545	19970528
		CIP of	US 1997-884479	19970627
		CIP of	US 1997-899319	19970723
		CIP of	US 1997-900194	19970729
			US 1997-2147	19971231

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9920066	A	Based on	WO 9933847
US 6071965	A	CIP of	US 5672592
		CIP of	US 5795877
		CIP of	US 5804602
		CIP of	US 5824662
		CIP of	US 5863536

PRIORITY APPLN. INFO: US 1997-2147 19971231; US 1996-665775 19960617; US 1996-665776 19960617; US 1996-718703 19960927; US 1996-775586 19961231; US 1996-778733 19961231; US 1997-825997 19970404; US 1997-835572 19970409; US 1997-842360 19970424; US 1997-858985 19970527; US 1997-863624 19970527; US 1997-864545 19970528; US 1997-884479 19970627; US 1997-899319 19970723; US 1997-900194 19970729

AB WO 9933847 A UPAB: 20000712

NOVELTY - Phosphinyl-alkanoic acid derivatives, their salts, hydrates and prodrugs.

DETAILED DESCRIPTION - Phosphinyl-alkanoic acid derivatives of formula (I) and their salts, hydrates and prodrugs are new.

X = CR6R7, O or NR8;

R1 = 1-9C linear or branched alkyl, 2-9C linear or branched alkenyl, 3-8C cycloalkyl, 5-9C cycloalkenyl or Ar, optionally substituted by one or more of carboxy, carbonyl, 3-8C cycloalkyl, 5-7C cycloalkenyl, halo, hydroxy, nitro, trifluoromethyl, 1-6C linear or branched alkyl, 2-6C linear or branched alkenyl, 1-9C alkoxy, 2-9C alkenyloxy, phenoxy, benzyloxy, amino or Ar;

R2-R8 = H or as R1;

Ar = 1- or 2-naphthyl; 2-, 3- or 4-indolyl; 2- or 3-furyl; tetrahydrofuranyl; tetrahydropyranyl; 2- or 3-thienyl; 2-, 3- or 4-pyridyl; benzyl or phenyl, all optionally substituted by one or more of carboxy, carbonyl, halo, hydroxy, nitro, trifluoromethyl, 1-6C linear or branched alkyl or alkoxy, 2-6C linear or branched alkenyl or alkenyloxy, phenoxy, benzyloxy or amino;

provided that:

if X = methylene, R1 = ethylene, R2 = 2-benzyloxycarbonylethyl, R3 = benzyl and R4 = H then R5 is not benzyl; and

if X = methylene, R1 = ethylene, R2 = 2-carboxyethyl, R3 and R4 = H, then R5 is not H.

An INDEPENDENT CLAIM is included for a pharmaceutical composition containing (I), or the two compounds excluded by the provisos, plus a carrier.

ACTIVITY - Anti-epileptic; analgesic; anti-ischemic; neurotropic; neuroprotective; anti-addictive; anticancer; antiproliferative.

Rats were subjected to transient ischemia by occlusion of the middle cerebral artery and treated, intraperitoneally before occlusion, with 100 mg/kg of 2-(phosphonomethyl)pentanedioic acid, then with 20 mg/kg/hour of the same compound. This treatment significantly reduced extracellular glutamate levels in the striatum and practically normalized the levels in the parietal cortex, but did not effect levels in the front cortex.

MECHANISM OF ACTION - (I) are inhibitors of the enzyme NAALADase (N-acetylated alpha -linked acidic dipeptidase) that converts N-acetylaspartyl-glutamate to glutamate, so they modulate levels of glutamate.

2-(((2-caboxypropyl)hydroxyphosphinyl)methyl)pentadioic acid (Ia) had in vitro inhibition constant against NAALADase of 1.5 nM.

USE - (I) and the excluded compounds are used: (i) to treat glutamate abnormalities (e.g. epilepsy, stroke, Alzheimer's, **Parkinson**'s or Huntington's diseases, amyotrophic lateral sclerosis, chronic pain,

ischemia, peripheral neuropathy, traumatic brain injury, and physical trauma to the spinal cord); (ii) to affect neuron activity (particularly to stimulate damaged neurons, promote neuron regeneration, prevent neurodegeneration and treat neurological disease, e.g. Guillain-Barre syndrome, multiple sclerosis and neurodegenerative diseases of (i)); (iii) to **treat** compulsive disorders (especially alcohol, **nicotine** or other dependences, eating disorders, pathological gambling, attention deficit or **Tourette**'s syndrome); (iv) to treat prostatic disease (specifically cancer or benign hypertrophy); and (v), excluding the known compounds, for inhibiting NAALADase. (I) can be used to treat a wide range of cancers, other than those of the prostate. Dwg.0/19

L207 ANSWER 54 OF 61 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1998-110348 [10] WPIDS
CROSS REFERENCE: 1998-145216 [13]
DOC. NO. CPI: C1998-036259
TITLE: Use of nicotine or its derivatives or metabolites - for treating e.g. inflammatory skin conditions, schizophrenia or Parkinson's disease.
DERWENT CLASS: A96 B03
INVENTOR(S): EVANS, B K; RHODES, J; RHODES, P; SANDBORN, W J
PATENT ASSIGNEE(S): (MAYO-N) MAYO FOUND MEDICAL EDUCATIONAL RES; (MAYO-N) MAYO FOUNDATION; (MAYO-N) MAYO FOUND MEDICAL EDUCATION & RES
COUNTRY COUNT: 79
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9802188	A1	19980122	(199810)*	EN	37
RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW					
AU 9735533	A	19980209	(199823)		
EP 954337	A1	19991110	(199952)	EN	
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
AU 718052	B	20000406	(200027)		
JP 2000515510	W	20001121	(200064)		32
US 6238689	B1	20010529	(200132)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9802188	A1	WO 1997-GB1938	19970716
AU 9735533	A	AU 1997-35533	19970716
EP 954337	A1	EP 1997-931953	19970716
		WO 1997-GB1938	19970716
AU 718052	B	AU 1997-35533	19970716
JP 2000515510	W	WO 1997-GB1938	19970716
		JP 1998-505766	19970716
US 6238689	B1	WO 1997-GB1938	19970716
		US 1999-147516	19990430

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9735533	A	Based on	WO 9802188

EP 954337	A1	Based on	WO 9802188
AU 718052	B	Previous Publ.	AU 9735533
		Based on	WO 9802188
JP 2000515510	W	Based on	WO 9802188
US 6238689	B1	Based on	WO 9802188

PRIORITY APPLN. INFO: GB 1996-14902 19960716

AB WO 9802188 A UPAB: 20010611

Use of nicotine and its derivatives or metabolites in a medicament adapted for absorption from the small and/or large intestine for the treatment or prophylaxis of inflammatory skin conditions, schizophrenia, Alzheimer's disease, Parkinson's disease, Tourettes syndrome, depression or to assist in the cessation of smoking, is new.

ADVANTAGE - The nicotine is delivered for absorption from the colon as a nicotine-polyacrylate complex in a sustained and delayed release enteric coated capsule. In this way, the high peak plasma levels, which normally cause side-effects associated with nicotine are reduced.

Dwg.0/6

L207 ANSWER 55 OF 61 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1995-022416 [03] WPIDS

DOC. NO. CPI: C1995-010316

TITLE: Nasal drug delivery compsn. for nicotine - provides a rapidly adsorbed pulse and sustained release and is useful as a nicotine replacement for smokers and for other therapeutic uses.

DERWENT CLASS: A96 B03

INVENTOR(S): ILLUM, L

PATENT ASSIGNEE(S): (DANB-N) DANBIOSYST UK LTD

COUNTRY COUNT: 54

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9427576	A1	19941208	(199503)*	EN	33
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE					
W: AT AU BB BG BR BY CA CH CN CZ DE DK ES FI GB GE HU JP KG KP KR KZ LK LU LV MD MG MN MW NL NO NZ PL PT RO RU SD SE SI SK TJ TT UA US UZ VN					
AU 9467272	A	19941220	(199512)		
NO 9504582	A	19951114	(199606)		
GB 2292316	A	19960221	(199611)		1
EP 697858	A1	19960228	(199613)	EN	
R: AT BE CH DE DK ES FR GB GR IE IT LI NL PT SE					
FI 9505583	A	19960119	(199615)		
JP 08510467	W	19961105	(199708)		29
GB 2292316	B	19970326	(199716)		
EP 697858	B1	19971022	(199747)	EN	12
R: AT BE CH DE DK ES FR GR IE IT LI NL PT SE					
DE 69406440	E	19971127	(199802)		
AU 685458	B	19980122	(199811)		
ES 2111304	T3	19980301	(199815)		
US 5935604	A	19990810	(199938)		
NO 306847	B1	20000103	(200008)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9427576	A1	WO 1994-GB1092	19940520
AU 9467272	A	AU 1994-67272	19940520
		WO 1994-GB1092	19940520
NO 9504582	A	WO 1994-GB1092	19940520

		NO 1995-4582	19951114
GB 2292316	A	WO 1994-GB1092	19940520
		GB 1995-23372	19951116
EP 697858	A1	EP 1994-915637	19940520
		WO 1994-GB1092	19940520
FI 9505583	A	WO 1994-GB1092	19940520
		FI 1995-5583	19951120
JP 08510467	W	WO 1994-GB1092	19940520
		JP 1995-500356	19940520
GB 2292316	B	WO 1994-GB1092	19940520
		GB 1995-23372	19951116
EP 697858	B1	EP 1994-915637	19940520
		WO 1994-GB1092	19940520
DE 69406440	E	DE 1994-606440	19940520
		EP 1994-915637	19940520
		WO 1994-GB1092	19940520
AU 685458	B	AU 1994-67272	19940520
ES 2111304	T3	EP 1994-915637	19940520
US 5935604	A	WO 1994-GB1092	19940520
		US 1996-553401	19960701
NO 306847	B1	WO 1994-GB1092	19940520
		NO 1995-4582	19951114

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9467272	A	Based on	WO 9427576
GB 2292316	A	Based on	WO 9427576
EP 697858	A1	Based on	WO 9427576
JP 08510467	W	Based on	WO 9427576
GB 2292316	B	Based on	WO 9427576
EP 697858	B1	Based on	WO 9427576
DE 69406440	E	Based on	EP 697858
		Based on	WO 9427576
AU 685458	B	Previous Publ.	AU 9467272
		Based on	WO 9427576
ES 2111304	T3	Based on	EP 697858
US 5935604	A	Based on	WO 9427576
NO 306847	B1	Previous Publ.	NO 9504582

PRIORITY APPLN. INFO: GB 1993-10412 19930520

AB WO 9427576 A UPAB: 19950126

A nasal drug delivery compsn. for nicotine is new. The compsn. contains nicotine or a deriv. or salt and delivers a pulse of nicotine for rapid adsorption and a controlled release of nicotine for subsequent sustained adsorption.

The compsn. may also include an ion-exchange material (e.g. microspheres (of carboxylated starch alginate or albumin-heparin conjugates) or a polymer contg. ionisable gps. (e.g. of gellan, alginate or a mixt.)) which forms a complex with nicotine and provides a controlled release. The compsn. also contains non ion-exchange microspheres to provide the pulse release of nicotine. The ion-exchange material may be a bioadhesive. The compsn. may contain sufficient nicotine to overload the ion-exchange material such that the excess nicotine is delivered as a pulse.

USE - The compsn. provides a profile of nicotine adsorption which mimics cigarette smoking much more closely than prior art compsns. It is therefore much more effective in **nicotine** replacement **therapy**. The compsn. can also be used when **nicotine** is required for **therapeutic** purposes, e.g. as a cognitive enhancer in ulcerative colitis, weight reduction, **Parkinson**'s disease, Alzheimer's disease, narcolepsy, depression and sleep apnoea. Pref. dosage

is 0.2 to 3 mg (pref. 1 mg) in the initial pulse and 5 to 20 mg (pref. 10 mg) by sustained release.
Dwg.0/3

L207 ANSWER 56 OF 61 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1993-257919 [32] WPIDS
DOC. NO. CPI: C1993-114547
TITLE: Nicotinoyl-alkyl di alkylamine(s) e.g. pseudo-oxy-**nicotine** - are used in **treatment** of neuro degenerative disorders e.g. **Parkinsonism** and senile dementia of Alzheimer's type.
DERWENT CLASS: B03
INVENTOR(S): CALDWELL, W S; LIPPIELLO, P M
PATENT ASSIGNEE(S): (RETO) REYNOLDS TOBACCO CO R J
COUNTRY COUNT: 18
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 5232932	A	19930803	(199332)*		5
EP 571139	A1	19931124	(199347)	EN	7
R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE					
JP 06032735	A	19940208	(199410)		5
EP 571139	B1	19950802	(199535)	EN	7
R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE					
DE 69300321	E	19950907	(199541)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 5232932	A	US 1992-887192	19920521
EP 571139	A1	EP 1993-303746	19930514
JP 06032735	A	JP 1993-134114	19930513
EP 571139	B1	EP 1993-303746	19930514
DE 69300321	E	DE 1993-600321	19930514
		EP 1993-303746	19930514

FILING DETAILS:

PATENT NO	KIND		PATENT NO
DE 69300321	E	Based on	EP 571139

PRIORITY APPLN. INFO: US 1992-887192 19920521
AB US 5232932 A UPAB: 19931118
Treatment of neurodegenerative disease, comprises admin. of a nicotinoylalkyl dialkylamine of formula (I). R, R1 = H or alkyl; X = halo or alkyl; n = 0-4; and p = 1-5.

A pref. (I) has n = O, p = 3, R = H; and R1 = Me and is also known as pseudooxynicotine (Ia).

USE - (I) can pass the blood/brain barrier and enter the CNS. They have nicotinic function, causing secretion and release of acetylcholine, dopamine, and other neurotransmitters. (I) are useful in Parkinson's disease and in senile dementia of Alzheimer type. Dosage is 5-150 mcg/kg, or 0.1-10 mg/hr per patient.

In a test of inhibition of L-(3H)-nicotine binding in mouse brain homogenate, (Ia) had IC50 = 1700nM. Dopamine release was measured on rat brain synaptosome homogenate, and was 45% of that provided by (S)-(-)-nicotine.
Dwg.0/0

L207 ANSWER 57 OF 61 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1993-235155 [29] WPIDS
DOC. NO. CPI: C1993-104846
TITLE: Treatment of neuro-degenerative diseases e.g. Alzheimer's and Parkinson's disease - using (R)-(+)-nicotine compounds which can bind to and activate nicotinic cholinergic receptors of brain.
DERWENT CLASS: B03
INVENTOR(S): CALDWELL, W S; LIPPIELLO, P M
PATENT ASSIGNEE(S): (RETO) REYNOLDS TOBACCO CO R J
COUNTRY COUNT: 18
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 5227391	A	19930713	(199329)*		5
EP 568208	A1	19931103	(199344)	EN	7
R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE					
JP 06024985	A	19940201	(199409)		5

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 5227391	A	US 1992-866596	19920410
EP 568208	A1	EP 1993-302730	19930407
JP 06024985	A	JP 1993-87875	19930324

PRIORITY APPLN. INFO: US 1992-866596 19920410
AB US 5227391 A UPAB: 19931116
The treatment of Alzheimer's type senile dementia, Parkinson's disease and other neurodegenerative diseases comprises administering an (R)-(+)-nicotine deriv. of formula (I). R = H or alkyl; R' = alkyl; X = halogen or alkyl; m = 0-4; n = 0-7.

In (I), pref. R = H or 1-7C alkyl, X = halogen or 1-7C alkyl and n = 0-3. Esp. R = Me.

USE/ADVANTAGE - (I) are able to bind to and hence cause activation of nicotinic cholinergic receptors of the brain and thus act as nicotinic agonists. (I) elicit neutrotransmitter secretion from nerve ending preparations (i.e. Synaptosomes) and cause relevant neurons to release or secrete acetyl choline, dopamine and other neutrotransmitterse. Thus they can be used to treat neurodegenerative diseases, Alzheimer's and Parkinson's. Suitable doses are 5-150 micro g/kg or 0.10-10 micro g/hr/patient.

Dwg. 0/0

L207 ANSWER 58 OF 61 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1993-075757 [09] WPIDS
DOC. NO. CPI: C1993-033399
TITLE: Use of cotinine and its derivs. - to treat neuro degenerative diseases such as Alzheimer's disease and Parkinson's disease.
DERWENT CLASS: B03
INVENTOR(S): CALDWELL, W S; LIPPIELLO, P M
PATENT ASSIGNEE(S): (RETO) REYNOLDS TOBACCO CO R J
COUNTRY COUNT: 18
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 5187169	A	19930216	(199309)*		5
EP 567703	A1	19931103	(199344)	EN	7
R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE					

JP 05286858 A 19931102 (199348) 5

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 5187169	A	US 1992-866698	19920410
EP 567703	A1	EP 1992-309793	19921026
JP 05286858	A	JP 1992-314452	19921030

PRIORITY APPLN. INFO: US 1992-866698 19920410

AB US 5187169 A UPAB: 19931119

Method for treating a patient suffering from a neurodegenerative disease, comprises admin. of a cotinine deriv. of formula (I) where R = H, or alkyl; R1 = alkyl, alkoxy or OH; X = halo or alkyl; m = 0-4; and n = 0-5.

The most pref. cpd. is cotinine itself (R = CH3).

USE/ADVANTAGE - (I) cause relevant neurons to secrete and/or release acetyl choline dopamine and other neurotransmitters, thereby showing a nicotinic function but avoiding use of **nicotine**. (I) are used in **treatment** of senile dementia of Alzheimer type and in **Parkinsons** disease, as specific examples. Dosage for humans is 5-150 mcg/kg or 0.10-10 mg/hr.

0/0

Dwg.0/0

L207 ANSWER 59 OF 61 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1993-338288 [43] WPIDS
DOC. NO. CPI: C1993-149602
TITLE: Use of anabasine and unsatd. **nicotine** cpds. - for **treating** neuro-degenerative diseases, esp. Alzheimer's and **Parkinson**'s disease.
DERWENT CLASS: B03
INVENTOR(S): CALDWELL, W S; LIPPIELLO, P M
PATENT ASSIGNEE(S): (RETO) REYNOLDS TOBACCO CO R J
COUNTRY COUNT: 18
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 567251	A1	19931027	(199343)*	EN	10
US 5276043	A	19940104	(199402)		6
JP 06009397	A	19940118	(199408)		7
EP 567251	B1	19961106	(199649)	EN	14
R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE					
DE 69305776	E	19961212	(199704)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
EP 567251	A1		EP 1993-302729	19930407
US 5276043	A	CIP of	US 1992-866597	19920410
			US 1993-23940	19930312
JP 06009397	A		JP 1993-96460	19930401
EP 567251	B1		EP 1993-302729	19930407
DE 69305776	E		DE 1993-605776	19930407
			EP 1993-302729	19930407

FILING DETAILS:

PATENT NO	KIND	PATENT NO

DE 69305776 E Based on EP 567251

PRIORITY APPLN. INFO: US 1992-866597 19920410; US 1993-23940 19930312

AB EP 567251 A UPAB: 19931207
Anabasive cpds. (opt. unsatd.) and unsatd. nicotine cpds. of formula (I) can be used to mfr. medicaments for treating neurodegenerative diseases. In (I), A=(I) or (II); mug (a) has 0, 1 or 2 conjugated ezc double bonds; ring (b) has 0,10 conjugated double bonds. A= and R11 are absent, or are R H or alkyl; R1 = alkyl; X = halogen or alkyl, m = 0-4 if A = (a), (c), (d) or (e), and m = 1-4 A=(b); N = 0-6.
USE/ADVANTAGE - (I) can act as agonists to activate nicotinic receptors and elicit neurotransmitter secretion. (II) can also increase the number of nicotinic cholinergic receptors of the brain of the patient and exhibit neuroprotective effects. They can therefore be used to treat patients with neurodegenerative diseases esp. those which cause a cholinergic deficit, esp. pref. senile dementia of Alzheimer's type or Parkinson's disease. Suitable are 5-150 mg/kg or 0.10-10 mg/hr/patient.
Dwg.0/0

L207 ANSWER 60 OF 61 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1993-282311 [36] WPIDS
DOC. NO. CPI: C1993-125952
TITLE: Substd. **nicotine** cpds. - for **treating** neurodegenerative diseases e.g Alzheimer's, senile dementia or **Parkinson**'s disease.
DERWENT CLASS: B03
INVENTOR(S): CALDWELL, W S; LIPPIELLO, P M
PATENT ASSIGNEE(S): (RETO) REYNOLDS TOBACCO CO R J
COUNTRY COUNT: 18
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 559495	A1	19930908	(199336)*	EN	7
R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE					
US 5242935	A	19930907	(199337)		5
JP 06024984	A	19940201	(199409)		5

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 559495	A1	EP 1993-301695	19930305
US 5242935	A	US 1992-847792	19920306
JP 06024984	A	JP 1993-64833	19930302

PRIORITY APPLN. INFO: US 1992-847792 19920306
AB EP 559495 A UPAB: 19931122
The use of substd. nicotine cpds. of formula (I) in the treatment of neurodegenerative diseases is new. R = H or alkyl; R1 = alkyl; X = halo or alkyl; n = 0-4; m = 0-3 with the proviso that n+m is at least 1.
USE - (I) are used for treating neurodegenerative diseases esp. Senile dementia of the Alzheimer's type or Parkinson's disease (claimed). Admin. may be by various routes e.g. inhalation, oral, i.v. or transdermal. Dosage is 5-150 microg/kg and is administered at a rate of 0.1-10 mg/hr/patient.

L207 ANSWER 61 OF 61 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1993-282243 [36] WPIDS
DOC. NO. CPI: C1993-125929
TITLE: Opt. substd. gamma-**nicotine** cpds. used to

treat neuro-degenerative diseases - e.g. senile dementia of Alzheimer's type and **Parkinson**'s disease.

DERWENT CLASS: B03
INVENTOR(S): CALDWELL, W S; LIPPIELLO, P M
PATENT ASSIGNEE(S): (RETO) REYNOLDS TOBACCO CO R J
COUNTRY COUNT: 18
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 559414	A1	19930908	(199336)*	EN	8
R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE					
US 5242934	A	19930907	(199337)		5
JP 06009398	A	19940118	(199408)		5

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 559414	A1	EP 1993-301535	19930301
US 5242934	A	US 1992-844332	19920302
JP 06009398	A	JP 1993-62488	19930301

PRIORITY APPLN. INFO: US 1992-844332 19920302

AB EP 559414 A UPAB: 19931122
The use of gamma nicotine cpds. of formula (I) for the treatment of neurodegenerative diseases is new. In (I), R = H or alkyl and the C. atoms on either ring may be opt. substd.

The pyridine ring pref. contains one or more halo or 1-5C alkyl substits. and the pyrrolidine ring may have one or more 1-5C alkyl substits.

USE - (I) are used for treating neurodegenerative diseases, esp. senile dementia of the Alzheimer's type and Parkinson's disease (claimed). Admin. may be various routes e.g. inhalation, oral, i.v. or transdermal. Dosage is 5-150 micro-g/kg and is administered at a rate of 0.1-10 mg/hr/patient.
Dwg.0/0

National Library of Medicine - Medical Subject Headings

2002 MeSH

MeSH Descriptor Data

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MeSH Heading	Biperiden
Tree Number	D02.455.426.100.080.100
Tree Number	D03.383.621.110
Scope Note	A muscarinic antagonist that has effects in both the central and peripheral nervous systems. It has been used in the treatment of arteriosclerotic, idiopathic, and postencephalitic parkinsonism. It has also been used to alleviate extrapyramidal symptoms induced by phenothiazine derivatives and reserpine.
Entry Term	Akineton
Entry Term	Biperiden Hydrochloride
Entry Term	Biperiden, 1R-(1 alpha,2 alpha(R*),4 alpha)-Isomer
Entry Term	Biperiden, 1S-(1 alpha,2 alpha(R*),4 alpha)-Isomer
Entry Term	Biperidene
Entry Term	alpha-Bicyclo(2.2.1)hept-5-en-2-yl-alpha-phenyl-1-piperidinepropanol
Allowable Qualifiers	AA AD AE AG AI AN BL CF CH CL CS CT DU EC HI IM IP ME PD PK PO RE SD ST TO TU UR
Pharm. Action	Antiparkinson Agents
Pharm. Action	Muscarinic Antagonists
Pharm. Action	Parasympatholytics
CAS Type 1 Name	1-Piperidinepropanol, alpha-bicyclo(2.2.1)hept-5-en-2-yl-alpha-phenyl-
Registry Number	514-65-8
Related Number	106347-58-4 (1R-(1 alpha,2 alpha(R*),4 alpha)-isomer)
Related Number	119542-35-7 (1S-(1 alpha,2 alpha(R*),4 alpha)-isomer)
Related Number	1235-82-1 (HCl)
History Note	91(66); was see under PIPERIDINES 1966-90
Unique ID	D001712

MeSH Tree Structures

National Library of Medicine - Medical Subject Headings

2002 MeSH

MeSH Descriptor Data

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MeSH Heading	Bromocriptine
Tree Number	D03.132.327.412.100
Tree Number	D03.549.439.131
Tree Number	D03.549.562.100
Scope Note	A semisynthetic ergotamine alkaloid that is a dopamine D2 agonist. It suppresses prolactin secretion.
Entry Term	2-Bromoergocryptine
Entry Term	Bromocryptin
Entry Term	2-Bromo-alpha-ergocryptine
Entry Term	2-Bromo-alpha-ergokryptine
Entry Term	2-Bromoergocryptine Mesylate
Entry Term	2-Bromoergocryptine Methanesulfonate
Entry Term	2-Bromoergokryptine
Entry Term	Bromocriptin
Entry Term	Bromocriptine Mesylate
Entry Term	CB-154
Entry Term	Parlodel
Allowable Qualifiers	AA AD AE AG AI AN BL CF CH CL CS CT DU EC HI IM IP ME PD PK PO RE SD ST TO TU UR
Pharm. Action	Antiparkinson Agents
Pharm. Action	Dopamine Agonists
Pharm. Action	Hormone Antagonists
CAS Type 1 Name	Ergotaman-3',6',18-trione, 2-bromo-12'-hydroxy-2'-(1-methylethyl)-5'alpha-(2 -methylpropyl)-
Registry Number	25614-03-3
Related Number	22260-51-1 (mesylate (salt))
Previous Indexing	Ergot Alkaloids (1966-1974)
Online Note	use BROMOCRIPTINE to search 2-BROMOERGOCRYPTINE 1975-80
History Note	81; was 2-BROMOERGOCRYPTINE 1978-80, was 2-BROMOERGOCRYPTINE see under ERGOTOXINE 1977, was 2-BROMOERGOCRYPTINE see under ERGOLINES 1975-76
Unique ID	D001971